

Supporting Information

Photocatalytic Reductive Fluoroalkylation of Nitrones

Vyacheslav I. Supranovich, Vitalij V. Levin, Marina I. Struchkova, Alexander D. Dilman*
N. D. Zelinsky Institute of Organic Chemistry, 119991 Moscow, Leninsky prosp. 47, Russian Federation
adil25@mail.ru

Content	
	Page
General Methods	S1
Synthesis of compounds 3a-z,π,σ and 6a-h	S2
Compounds 3a-z,π,σ	S3-S12
Compounds 6a-h	S13-S15
Synthesis of compounds 7a-c	S15
Compounds 7a-c	S16
NMR spectra	S17-S133

General Methods: All reactions were performed under an argon atmosphere. Column chromatography was carried out employing silica gel (230-400 mesh). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography visualizing with UV and/or acidic aq. KMnO₄ solution. High resolution mass spectra (HRMS) were measured using electrospray ionization (ESI) and time-of-flight (TOF) mass analyzer. The measurements were done in a positive ion mode (interface capillary voltage –4500 V) or in a negative ion mode (3200 V); mass range from m/z 50 to m/z 3000. For irradiation, a strip of light emitting diodes (2835-120LED 1M-Blue, 12V) was used.

Reagents. The following starting compounds were prepared according to literature procedures: *N*-(benzylidene)methylamine *N*-oxide (**1a**),¹ *N*-(benzylidene)benzylamine *N*-oxide,² 3,4-dihydroisoquinoline *N*-oxide,² *N*-(benzylidene)-*tert*-butylamine *N*-oxide,² *N*-(2-methylpropylidene)benzylamine *N*-oxide,³ *N*-(2-pyridylidene)methylamine *N*-oxide,⁴ *N*-methyl-(2,2-dimethylpropylidene)amine *N*-oxide,⁵ *N*-[4-(methoxycarbonyl)benzylidene]methanamine *N*-oxide,⁶ *N*-(3-phenylpropylidene)methanamine *N*-oxide,⁷ *N*-(4-methoxybenzylidene)methanamine *N*-oxide,⁸ *N*-(4-cyanobenzylidene)methanamine *N*-oxide,⁹ *N*-(2-hydroxybenzylidene)methanamine *N*-oxide,¹⁰ (2,2-difluoro-2-iodoethyl)benzene (**2a**),¹¹ for trifluoromethyl and pentafluoroethyl iodides, solutions in DMSO were used.¹²

Fluoroalkylation of nitrones **1**. Synthesis of compounds **3a-z,π,σ** and **6a-h** (General Procedure).

Photocatalyst Ir(ppy)₂(dtbbpy)PF₆ (2.3 mg, 0.0025 mmol), nitrone **1** (0.50 mmol), and ascorbic acid (132 mg, 0.75 mmol) were placed in a tube containing a stirring bar. The tube was evacuated and filled with argon. DMSO (1 mL) was added followed by amine [for **3a,π** NEt₃, 76 mg, 0.75 mmol; for **3b-z,σ**, 2,4,6-collidine, 91 mg, 0.75 mmol; for **6a-h**, morpholine, 109 mg, 1.25 mmol) and fluoralkyl iodide (for **3a-p,r,s,z,π,σ**, **6a-d,f-h**, 0.75 mmol; for **3q,t-y**, **6e**, 0.50 mmol). The reaction vessel was irradiated by a strip of blue LEDs with water cooling to maintain reaction temperature around 23–25 °C for 2 hours. For the work-up, the mixture was treated with water (10 mL) and extracted with EtOAc (3×4 mL). The combined organic phases were dried with Na₂SO₄ and concentrated under vacuum, and the residue was purified by column chromatography.

Trifluoromethylation of nitrone **1a** (representative example on 1 mmol scale).

Photocatalyst Ir(ppy)₂(dtbbpy)PF₆ (4.6 mg, 0.005 mmol), nitrone **1a** (135 mg, 1.0 mmol), and ascorbic acid (264 mg, 1.5 mmol) were placed in a tube containing a stirring bar. The tube was evacuated and filled with argon. DMSO (2 mL) was added followed by 2,4,6-collidine (182 mg, 1.5 mmol) and a solution of CF₃I (528 mg of 56% solution in DMSO, 1.5 mmol). The reaction vessel was irradiated by a strip of blue LEDs with water cooling to maintain reaction temperature around 23–25 °C for 2 hours. For the work-up, the mixture was treated with water (10 mL) and extracted with EtOAc (3×4 mL). The combined organic phases were dried with Na₂SO₄ and concentrated under vacuum, and the residue was purified by column chromatography eluting with hexanes/EtOAc, 5/1, affording 154 mg (75% yield) of compound **3b**.

¹ Tyrrell, E.; Allen, J.; Jones, K.; Beauchet, R. *Synthesis* **2005**, 2393–2399.

² Murahashi, S.; Mitsui, H.; Shiota, T.; Tsuda, T.; Watanabe, S. *J. Org. Chem.* **1990**, *55*, 1736–1744.

³ Dondoni, A.; Franco, S.; Junquera, F.; Merchán, F. L.; Merino, P.; Tejero, T. *Synth. Commun.* **1994**, *24*, 2537–2550.

⁴ Shimizu, T.; Ishizaki, M.; Nitada, N. *Chem. Pharm. Bull.* **2002**, *50*, 908–921.

⁵ Aurich, H. G.; Franzke, M.; Kesselheim, H. P.; Rohr, M. *Tetrahedron* **1992**, *48*, 669–682.

⁶ Yoshimura, F.; Abe, T.; Tanino, K. *Synlett* **2014**, *25*, 1863–1868.

⁷ Zheng, H.; McDonald, R.; Hall, D. G. *Chem. A Eur. J.* **2010**, *16*, 5454–5460.

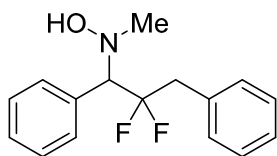
⁸ Yakura, T.; Nakazawa, M.; Takino, T.; Ikeda, M. *Chem. Pharm. Bull.* **1992**, *40*, 2014–2018.

⁹ Chan, K. S.; Yeung, M. L.; Chan, W.; Wang, R.; Mak, T. C. W. *J. Org. Chem.* **1995**, *60*, 1741–1747.

¹⁰ Chen, S.; Zhao, K.; Chen, G. *J. Chem.* **2015**, *2015*, 1–6.

¹¹ Levin, V. V.; Zemtsov, A. A.; Struchkova, M. I.; Dilman, A. D. *Org. Lett.* **2013**, *15*, 917–919.

¹² Sladojevich, F.; McNeill, E.; Börgel, J.; Zheng, S.-L.; Ritter, T. *Angew. Chem. Int. Ed.* **2015**, *54*, 3712–3716.

***N*-(2,2-Difluoro-1,3-diphenylpropyl)-*N*-methylhydroxylamine (3a).**

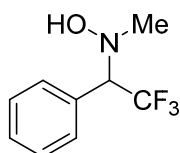
Yield 120 mg (86%). Colorless crystals. Mp 138–140 °C. Chromatography: hexanes/EtOAc, 4/1. R_f 0.24 (hexanes/EtOAc, 4/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.46–7.23 (m, 10H), 5.23 (s, 1H), 3.80 (t, J = 13.6 Hz, 1H), 3.38 (td, J = 17.2, 14.6 Hz, 1H), 3.20 (td, J = 17.2, 14.6 Hz, 1H), 2.56 (s, 3H).

^{13}C NMR (75 MHz, $\text{DMSO}-d_6$) δ : 133.8 (d, J = 4.0 Hz), 133.3, 131.5, 130.9, 128.3, 128.1, 127.9, 127.1, 123.6 (dd, J = 241.8, 250.2 Hz), 73.8 (dd, J = 22.1, 28.2 Hz), 46.5, 40.5 (t, J = 24.0 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : -100.9 (m).

HRMS (ESI): calcd for $\text{C}_{16}\text{H}_{18}\text{F}_2\text{NO}$ ($\text{M}+\text{H}$) 278.1351; found 278.1352.

***N*-Methyl-*N*-(2,2,2-trifluoro-1-phenylethyl)hydroxylamine (3b).**

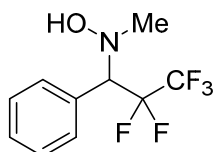
According to General Procedure, yield 84 mg (82%). Colorless crystals. Mp 112–113 °C. Chromatography: hexanes/EtOAc, 5/1. R_f 0.27 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.47–7.39 (m, 5H), 4.10 (q, J = 7.6 Hz, 1H), 2.57 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 131.2, 130.3, 129.5, 128.7, 124.9 (q, J = 281.8 Hz), 74.2 (q, J = 27.5 Hz), 46.4.

^{19}F NMR (282 MHz, CDCl_3) δ : -68.9 (d, J = 7.6 Hz).

HRMS (ESI): calcd for $\text{C}_9\text{H}_{11}\text{F}_3\text{NO}$ ($\text{M}+\text{H}$) 206.0787; found 206.0793.

***N*-Methyl-*N*-(2,2,3,3,3-pentafluoro-1-phenylpropyl)hydroxylamine (3c)**

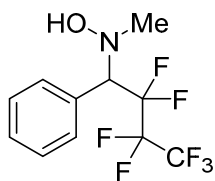
Yield 117 mg (92%). Colorless crystals. Mp 71–73 °C. Chromatography: hexanes/EtOAc, 7/1. R_f 0.38 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.54–7.39 (m, 5H), 5.44 (s, 1H), 4.16 (d, J = 17.5, 12.1 Hz, 1H), 2.54 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 131.7, 129.5, 129.0, 128.5, 119.3 (qt, J = 286.9, 35.8 Hz), 114.7 (ddq, J = 262.9, 255.7, 35.3 Hz), 71.2 (dd, J = 24.7, 18.4 Hz), 46.1.

^{19}F NMR (282 MHz, CDCl_3) δ : -82.7 (s, 3F), -116.2 (dd, J = 275.8, 11.7 Hz, 1F), -121.3 (dd, J = 275.8, 17.1 Hz, 1F).

HRMS (ESI): calcd for $\text{C}_{10}\text{H}_{11}\text{F}_5\text{NO}$ ($\text{M}+\text{H}$) 256.0755; found 256.0757.

***N*-(2,2,3,3,4,4,4-Heptafluoro-1-phenylbutyl)-*N*-methylhydroxylamine (3d).**

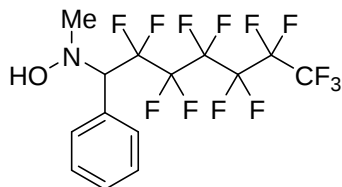
Yield 145 mg (94%). Colorless crystals. Mp 52–54 °C. Chromatography: hexanes/EtOAc, 1/5. R_f 0.30 (hexanes/EtOAc, 1/5).

^1H NMR (300 MHz, CDCl_3) δ : 7.57–7.40 (m, 5H), 5.77 (s, 1H), 4.28 (dd, J = 17.4, 12.2 Hz, 1H), 2.56 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 131.8, 129.5, 128.9, 128.4, 71.1 (dd, J = 24.8, 18.3 Hz), 45.9.

^{19}F NMR (282 MHz, CDCl_3) δ : -81.6 (t, J = 10.8 Hz, 3F), -113.8 (dm, J = 283.5 Hz, 1F), -118.2 (dm, J = 283.5 Hz, 1F), -126.1 (t, J = -5.9 Hz, 2F).

HRMS (ESI): calcd for $\text{C}_{11}\text{H}_{11}\text{F}_7\text{NO}$ ($\text{M}+\text{H}$) 306.0723; found 306.0728.

***N*-Methyl-*N*-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-1-phenylheptyl)hydroxylamine (3e).**

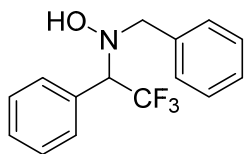
Yield 225 mg (99%). Colorless crystals. Mp 46–49 °C. Chromatography: hexanes/EtOAc, 10/1. R_f 0.30 (hexanes/EtOAc, 10/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.87–7.45 (m, 5H), 5.83 (br s, 1H), 4.35 (dd, J = 17.4, 12.2 Hz, 1H), 2.61 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 131.9, 129.5, 129.0, 128.4, 71.4 (dd, J = 25.2, 18.4 Hz), 46.0.

^{19}F NMR (282 MHz, CDCl_3) δ : -81.9 (t, J = 9.8 Hz, 3F), -112.9 (dm, J = 284.2 Hz, 1F), -117.6 (dm, J = 284.2 Hz, 1F), -121.9 (m, 2F), -122.8 (m, 2F), -123.7 (m, 2F), -127.2 (m, 2F).

HRMS (ESI): calcd for $\text{C}_{14}\text{H}_{11}\text{F}_{13}\text{NO}$ ($\text{M}+\text{H}$) 456.0628; found 456.0628.

***N*-Benzyl-*N*-(2,2,2-trifluoro-1-phenylethyl)hydroxylamine (3f).**

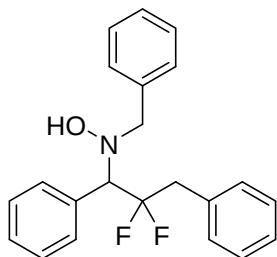
Yield 127 mg (91%). Colorless crystals. Mp 83–84 °C. Chromatography: hexanes/EtOAc 5/1. R_f 0.36 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.60–7.32 (m, 10H), 5.27 (s, 1H), 4.32 (q, J = 7.8 Hz, 1H), 3.90 (d, J = 13.2 Hz, 1H), 3.69 (d, J = 13.2 Hz, 1H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 136.9, 131.0, 130.6, 129.4, 129.4, 128.7, 128.6, 127.8, 125.1 (q, J = 281 Hz), 71.4 (q, J = 28.0 Hz), 61.7.

^{19}F NMR (282 MHz, CDCl_3) δ : -68.9 Hz (d, J = 7.8 Hz).

HRMS (ESI): calcd for $\text{C}_{15}\text{H}_{15}\text{F}_3\text{NO}$ ($\text{M}+\text{H}$) 282.1100; found 282.1102.

***N*-Benzyl-*N*-(2,2-difluoro-1,3-diphenylpropyl)hydroxylamine (3g).**

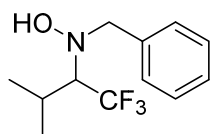
Yield 140 mg (79%). Colorless oil. Chromatography: hexanes/EtOAc, 6/1. R_f 0.38 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.66–7.33 (m, 15H), 5.13 (s, 1H), 4.08 (dd, J = 17.3, 10.4 Hz, 1H), 3.89 (d, J = 13.2 Hz, 1H), 3.68 (d, J = 13.2 Hz, 1H), 3.59–3.30 (m, 2H).

^{13}C NMR (50 MHz, CDCl_3) δ : 137.5, 133.2 (dd, J = 5.1, 3.0 Hz), 132.2, 131.6, 130.8, 129.5, 128.6, 128.4, 128.3, 128.2, 127.5, 127.3, 123.4 (dd, J = 250.7, 246.5 Hz), 71.9 (dd, J = 26.3, 22.9 Hz), 61.9, 41.9 (t, J = 24.9 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : -98.7 (dm, J = 252.2 Hz, 1F), -101.0 (dm, J = 252.2 Hz, 1F).

HRMS (ESI): calcd for $\text{C}_{22}\text{H}_{22}\text{F}_2\text{NO}$ ($\text{M}+\text{H}$) 354.1664; found 354.1668.

***N*-Benzyl-*N*-(1,1,1-trifluoro-3-methylbutan-2-yl)hydroxylamine (3h).**

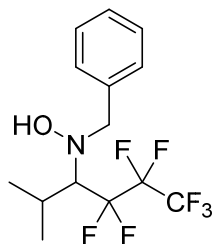
Yield 114 mg (92%). Colorless crystals. Mp 50–52 °C. Chromatography: hexanes/EtOAc, 5/1. R_f 0.30 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.41–7.32 (m, 5H), 4.89 (s, 1H), 4.23 (d, J = 13.4, 1H), 4.05 (d, J = 13.4, 1H), 3.06 (qd, J = 8.5, 6.9 Hz, 1H), 2.25 (octet, J = 6.9 Hz, 1H), 1.19 (d, J = 6.9 Hz, 3H), 1.15 (dd, J = 6.9, 1.4 Hz, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 138.0, 129.3, 128.6, 127.7, 126.7 (q, J = 289.6 Hz), 71.5 (q, J = 23.7 Hz), 61.8 (q, J = 1.6 Hz), 27.2 (q, J = 1.1 Hz), 21.3, 20.1 (q, J = 2.0 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : -64.3 (d, J = 8.5 Hz)

HRMS (ESI): calcd for $\text{C}_{12}\text{H}_{17}\text{F}_3\text{NO}$ ($\text{M}+\text{H}$) 248.1257; found 248.1255.

***N*-Benzyl-*N*-(4,4,5,5,6,6,6-heptafluoro-2-methylhexan-3-yl)hydroxylamine (3i).**

Yield 131 mg (75%). Colorless oil. Chromatography: hexanes/EtOAc, 8/1. R_f 0.50 (hexanes/EtOAc, 5/1).

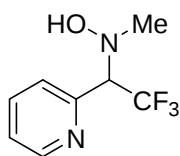
^1H NMR (300 MHz, CDCl_3) δ : 7.38–7.29 (m, 5H), 4.64 (s, 1H), 4.20 (d, J = 13.2 Hz, 1H), 3.97 (d, J = 13.2 Hz, 1H), 3.37 (dm, J = 23.9 Hz, 1H), 2.61 (dtd, J = 13.9, 7.0, 3.4 Hz), 1.29 (dt, J = 6.9, 1.9 Hz, 3H), 1.26 (dd, J = 7.2, 1.1 Hz, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 137.6, 129.3, 128.6, 127.8, -118.8 (dddd, J = 293.7, 258.2, 30.7, 25.9 Hz), -118.4 (qt, J = 288.2, 34.7 Hz), -109.8 (ddq, J = 268.4, 264.6, 37.0 Hz), 68.5 (dd, J = 24.9, 18.6 Hz), 62.7 (t, J = 2.1 Hz), 26.5, 22.9 (d, J = 3.3 Hz), 20.8 (t, J = 30.1 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : -81.3 (dd, J = 13.7, 8.6 Hz, 3F), -112.1 (dm, J = 287.4 Hz, 1F), -119.2 (dm, J = 287.4, 8.1 Hz, 1F), -123.9 (ddd, J = 286.9, 13.7, 8.0 Hz, 1F), -127.6 (dd, J = 286.8, 15.1 Hz, 1F).

HRMS (ESI): calcd for $\text{C}_{14}\text{H}_{17}\text{F}_7\text{NO}$ ($\text{M}+\text{H}$) 348.1193; found 348.1186.

***N*-Methyl-*N*-(2,2,2-trifluoro-1-(pyridin-2-yl)ethyl)hydroxylamine (3j).**



Yield 79 mg (77%). Colorless crystals. Mp 77–79 °C. Chromatography: hexanes/EtOAc, 1/1. R_f 0.30 (hexanes/EtOAc, 1/1).

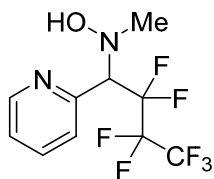
^1H NMR (300 MHz, CDCl_3) δ : 8.59 (d, J = 4.1 Hz, 1H), 7.79–7.71 (m, 2H), 7.60 (d, J = 7.7 Hz, 1H), 7.33 (t, J = 5.8 Hz, 1H), 4.44 (q, J = 7.7 Hz, 1H), 2.66 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 152.0, 149.0, 137.0, 125.2, 124.6 (q, J = 282.1), 124.1, 73.9 (q, J = 27.6 Hz), 46.5.

^{19}F NMR (282 MHz, CDCl_3) δ : -69.2 (d, J = 7.7 Hz).

HRMS (ESI): calcd for $\text{C}_8\text{H}_{10}\text{F}_3\text{N}_2\text{O}$ ($\text{M}+\text{H}$) 207.0740; found 207.0733.

***N*-(2,2,3,3,4,4,4-heptafluoro-1-(pyridin-2-yl)butyl)-*N*-methylhydroxylamine (3k)**



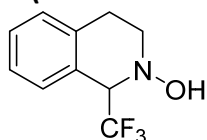
Yield 110 mg (72%). Colorless crystals. Mp 80–82 °C. Chromatography: hexanes/EtOAc, 2/1. R_f 0.32 (hexanes/EtOAc, 2/1).

^1H NMR (300 MHz, CDCl_3) δ : 8.59 (ddd, J = 4.9, 1.6, 0.9 Hz, 1H), 7.77–7.70 (m, 2H), 7.55 (s, 1H), 7.33 (ddd, J = 7.4, 4.9, 2.4 Hz, 1H), 4.58 (dd, J = 19.5, 10.3 Hz, 1H), 2.61 (s, 3H).

^{19}F NMR (282 MHz, CDCl_3) δ : -81.6 (dd, J = 12.4, 9.0 Hz, 3F), -112.8 (d, sept, J = 284.9, 11.9 Hz, 1F), -119.4 (dm, J = 284.9, 1F), -125.5 (ddd, J = 290.0, 12.1, 6.6 Hz, 1F), -127.4 (dd, J = 290.0, 12.6 Hz, 1F).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 150.9, 148.7, 136.7, 126.8, 124.2, 71.0 (dd, J = 25.6, 18.1 Hz), 46.3.

HRMS (ESI): calcd for $\text{C}_{10}\text{H}_{10}\text{F}_7\text{N}_2\text{O}$ ($\text{M}+\text{H}$) 307.0676; found 307.0666.

1-(Trifluoromethyl)-3,4-dihydroisoquinolin-2(1H)-ol (3l).

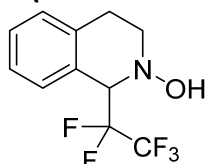
Yield 89 mg (82%). Colorless oil. Chromatography: hexanes/EtOAc, 5/1. R_f 0.28 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.42–7.22 (m, 5H), 4.77 (q, J = 7.7, 1H), 3.56 (dt, J = 11.3, 5.2 Hz, 1H), 3.27 (ddd, J = 11.3, 8.2, 4.7 Hz, 1H), 3.06–2.93 (m, 2H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 136.0, 128.8, 128.6, 128.4, 127.3, 126.6, 125.3 (q, J = 280.0 Hz), 68.6 (q, J = 27.0 Hz), 52.4, 26.4.

^{19}F NMR (282 MHz, CDCl_3) δ : –72.5 (d, J = 7.7 Hz).

HRMS (ESI): calcd for $\text{C}_{10}\text{H}_{11}\text{F}_3\text{NO}$ ($\text{M}+\text{H}$) 218.0787; found 218.0795.

1-(Perfluoroethyl)-3,4-dihydroisoquinolin-2(1H)-ol (3m).

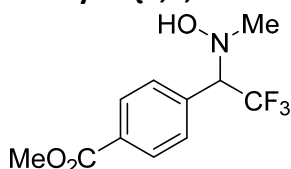
Yield 111 mg (83%). Colorless crystals. Mp 47–50 °C. Chromatography: hexanes/EtOAc, 5/1. R_f 0.38 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.39–7.22 (m, 4H), 5.99 (br. s, 1H), 4.81 (dd, J = 20.7, 8.4 Hz, 1H), 3.51–3.41 (m, 1H), 3.35–3.26 (m, 1H), 3.09 (ddd, J = 16.4, 8.2, 4.8 Hz, 1H), 2.82 (dt, J = 16.4, 5.4 Hz, 1H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 136.4, 129.4 (d, J = 4.9 Hz), 128.7, 128.5, 126.5, 126.3, 119.5 (qdd, J = 287.2, 36.9, 35.4 Hz), 114.1 (ddq, J = 260.2, 254.9, 35.3 Hz), 67.1 (t, J = 22.9 Hz), 51.2 (d, J = 2.5 Hz), 24.5.

^{19}F NMR (282 MHz, CDCl_3) δ : –81.4 (s, 3F), –112.8 (dd, J = 278.8, 8.7, 2.9 Hz, 1F), –122.2 (dd, J = 278.8, 20.9 Hz, 1F).

HRMS (ESI): calcd for $\text{C}_{11}\text{H}_{11}\text{F}_5\text{NO}$ ($\text{M}+\text{H}$) 268.0755; found 268.0742.

Methyl 4-{2,2,2-trifluoro-1-[hydroxy(methyl)amino]ethyl}benzoate (3n).

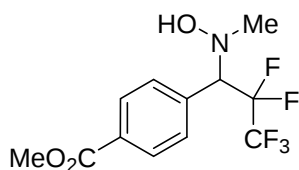
Yield 100 mg (76%). Colorless crystals. Mp 95–96 °C. Chromatography: hexanes/EtOAc, 3/1. R_f 0.24 (hexanes/EtOAc, 3/1).

^1H NMR (300 MHz, CDCl_3) δ : 8.05 (d, J = 8.2 Hz, 2H), 7.52 (d, J = 8.2 Hz, 2H), 6.45 (s, 1H), 4.15 (q, J = 7.5 Hz, 1H), 3.91 (s, 3H), 2.55 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 166.8, 135.9, 131.1, 130.4, 129.8, 124.5 (q, J = 281.7 Hz), 73.6 (q, J = 27.8 Hz), 52.4, 46.4.

^{19}F NMR (282 MHz, CDCl_3) δ : –68.9 (d, J = 7.1 Hz).

HRMS (ESI): calcd for $\text{C}_{11}\text{H}_{13}\text{F}_3\text{NO}_3$ ($\text{M}+\text{H}$) 264.0842; found 264.0838.

Methyl 4-{2,2,3,3,3-pentafluoro-1-[hydroxy(methyl)amino]propyl}benzoate (3o).

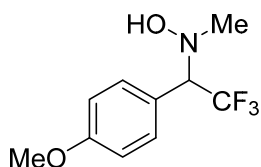
Yield 146 mg (93%). Colorless crystals. Mp 129–130 °C. Chromatography: hexanes/EtOAc, 4/1. R_f 0.22 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 8.06 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 8.3 Hz, 2H), 5.84 (s, 1H), 4.20 (dd, J = 17.8, 11.7 Hz, 1H), 3.91 (s, 3H), 2.51 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 166.9, 134.0, 131.8, 131.2, 129.5, 121.1 (qt, J = 287.0, 35.6 Hz), 114.4 (ddq, J = 263.7, 255.3, 35.6 Hz), 70.7 (dd, J = 25.2, 18.5 Hz), 52.4, 46.1.

^{19}F NMR (282 MHz, CDCl_3) δ : -82.8 (s, 3F), -115.9 (dd, J = 276.8, 11.3 Hz, 1F), -121.7 (dd, J = 276.8, 17.4 Hz, 1F)

HRMS (ESI): calcd for $\text{C}_{12}\text{H}_{13}\text{F}_5\text{NO}_3$ ($\text{M}+\text{H}$) 314.0810; found 314.0809.

Methyl 4-(2,2,3,3,3-pentafluoro-1-(hydroxy(methyl)amino)propyl)benzoate (3p).

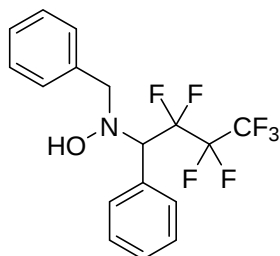
Yield 80 mg (68%). Colorless crystals. Mp 119–120 °C. Chromatography: hexanes/EtOAc, 3/1. R_f 0.28 (hexanes/EtOAc, 3/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.36 (d, J = 8.7 Hz, 2H), 6.92 (d, J = 8.7 Hz, 2H), 6.26 (s, 1H), 4.04 (q, J = 7.7 Hz, 1H), 3.82 (s, 3H), 2.55 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 160.4, 131.5, 125.0 (q, J = 281.6 Hz), 123.1, 114.1, 73.4 (q, J = 27.6 Hz), 55.4, 46.3.

^{19}F NMR (282 MHz, CDCl_3) δ : -69.3 (d, J = 7.7 Hz).

HRMS (ESI): calcd for $\text{C}_{10}\text{H}_{13}\text{F}_3\text{NO}_2$ ($\text{M}+\text{H}$) 236.0893; found 236.0894.

***N*-Benzyl-*N*-(2,2,3,3,4,4,4-heptafluoro-1-phenylbutyl)hydroxylamine (3q).**

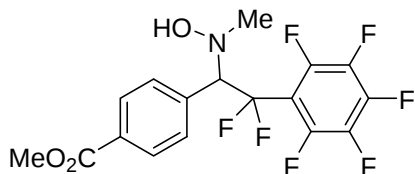
Yield 131 mg (69%). Colorless oil. Chromatography: hexanes/EtOAc, 10/1. R_f 0.50 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.70–7.35 (m, 10H), 5.03 (s, 1H), 4.48 (dd, J = 21.3, 8.9 Hz, 1H), 3.90 (d, J = 13.1 Hz, 1H), 3.76 (d, J = 13.1 Hz, 1H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 136.7, 132.1, 129.5, 129.4, 129.1, 128.6, 128.4, 127.9, 68.8 (dd, J = 27.2, 18.5 Hz), 62.0.

^{19}F NMR (282 MHz, CDCl_3) δ : -81.6 (dd, J = 13.0, 9.0 Hz, 3F), -111.5 (dm, J = 285.4, 1F), -119.0 (dm, J = 285.4,), -125.3 (ddd, J = 290.0, 13.4, 7.8 Hz, 1F), -127.4 (dd, J = 290.0, 14.8 Hz, 1F)
 HRMS (ESI): calcd for $\text{C}_{17}\text{H}_{15}\text{F}_7\text{NO}$ ($\text{M}+\text{H}$) 382.1036; found 382.1036.

Methyl 4-(2,2-difluoro-1-(hydroxy(methyl)amino)-2-(perfluorophenyl)ethyl)benzoate (3r)



Yield 169 mg (82%). Colorless crystals. Mp 114–117 °C. Chromatography: hexanes/EtOAc, 4/1. R_f 0.22 (hexanes/EtOAc, 5/1).

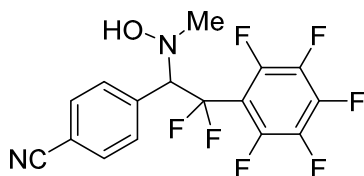
^1H NMR (300 MHz, CDCl_3) δ : 8.03 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.0 Hz, 2H), 5.76 (s, 1H), 4.26 (dd, J = 19.5, 7.8 Hz, 1H), 3.92 (s, 3H), 2.51 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 166.9, 144.7 (d, J = 256.1 Hz), 142.2 (d, J = 258.1 Hz), 137.8 (d, J = 249.2 Hz), 136.5, 131.2, 130.9, 129.6, 119.8 (dd, J = 258.2, 250.5 Hz), 111.9 (m), 76.3 (dd, J = 27.6, 22.4 Hz), 52.3, 46.8.

^{19}F NMR (282 MHz, CDCl_3) δ : -91.8 (dt, J = 272.1, 23.9 Hz, 1F), -101.2 (ddd, J = 272.1, 51.7, 30.7 Hz, 1F), -140.9-(-141.2) (m, 2F), -151.4 (t, J = 21.2 Hz, 1F), -161.5-(-161.7) (m, 2F).

HRMS (ESI): calcd for $\text{C}_{17}\text{H}_{13}\text{F}_7\text{NO}_3$ ($\text{M}+\text{H}$) 412.0778; found 412.0764.

4-(2,2-Difluoro-1-(hydroxy(methyl)amino)-2-(perfluorophenyl)ethyl)benzonitrile (3s).



Yield 170 mg (90%). Colorless crystals. Mp 109–112 °C. Chromatography: hexanes/EtOAc, 3/1. R_f 0.36 (hexanes/EtOAc, 3/1).

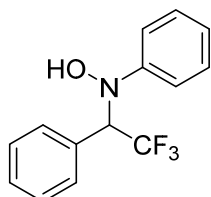
^1H NMR (300 MHz, CDCl_3) δ : 7.66 (s, 4H), 5.48 (br s, 1H), 4.21 (dd, J = 21.1, 6.1 Hz), 2.48 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 144.7 (d, J = 254.9 Hz), 142.3 (d, J = 258.3 Hz), 138.2 (d, J = 252.6 Hz), 136.4, 132.2, 132.0, 119.7 (dd, J = 259.1, 247.7 Hz), 118.4, 113.2, 111.5 (m), 75.8 (dd, J = 29.7, 21.5 Hz), 46.8.

^{19}F NMR (282 MHz, CDCl_3) δ : -89.4 (dt, J = 274.5 Hz, 23.6 Hz, 1F), -103.3 (dq, J = 275.3, 24.1 Hz, 1F), -140.9-(-140.3) (m, 2F), -151.0 (t, J = 21.0 Hz, 1F), -161.1-(-161.5) (m, 2F).

HRMS (ESI): calcd for $\text{C}_{16}\text{H}_{10}\text{F}_7\text{N}_2\text{O}$ ($\text{M}+\text{H}$) 379.0676; found 379.0662.

***N*-Phenyl-*N*-(2,2,2-trifluoro-1-phenylethyl)hydroxylamine (3t).¹³**



¹³ Nelson, D. W.; Owens, J.; Hiraldo, D. J. *Org. Chem.* **2001**, 66, 2572–2582.

Yield 89 mg (67%). Colorless crystals. Mp 77–78 °C. Chromatography: hexanes/EtOAc, 7/1. R_f 0.41 (hexanes/EtOAc, 5/1).

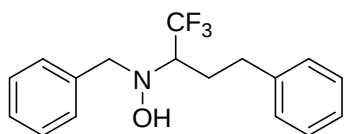
^1H NMR (300 MHz, CDCl_3) δ : 7.45–7.28 (m, 7H), 7.15–7.05 (m, 3H), 5.46 (s, 1H), 4.96 (q, J = 8.2 Hz, 1H)

^{13}C NMR (75.5 MHz, CDCl_3) δ : 150.5, 130.4, 129.4, 129.2, 128.9, 128.2, 125.1 (q, J = 282.4 Hz), 123.6, 118.0, 72.9 (q, J = 29.0 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : –69.6 (d, J = 8.2 Hz).

HRMS (ESI): calcd for $\text{C}_{14}\text{H}_{13}\text{F}_3\text{NO}$ ($\text{M}+\text{H}$) 268.0944; found 268.0943.

***N*-Benzyl-*N*-(1,1,1-trifluoro-4-phenylbutan-2-yl)hydroxylamine (3u).**



Yield 115 mg (74%). Colorless oil. Chromatography: hexanes/EtOAc, 7/1. R_f 0.42 (hexanes/EtOAc, 5/1).

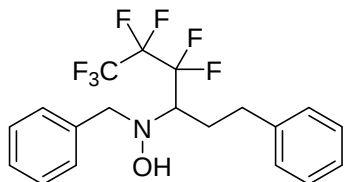
^1H NMR (300 MHz, CDCl_3) δ : 7.48–7.31 (m, 10H), 5.31 (s, 1H), 4.05 (m, 2H), 3.39–3.27 (m, 1H), 2.94 (t, J = 7.6 Hz, 2H), 2.42–2.30 (m, 1H), 2.26–2.14 (m, 1H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 141.0, 137.3, 129.4, 128.7, 128.6, 128.6, 127.7, 126.4 (J = 285.7 Hz), 126.4, 64.8 (q, J = 25.7 Hz), 61.2, 32.7, 26.0.

^{19}F NMR (282 MHz, CDCl_3) δ : –70.1 (d, J = 8.0 Hz).

HRMS (ESI): calcd for $\text{C}_{17}\text{H}_{19}\text{F}_3\text{NO}$ ($\text{M}+\text{H}$) 310.1413; found 310.1419.

***N*-benzyl-*N*-(4,4,5,5,6,6,6-heptafluoro-1-phenylhexan-3-yl)hydroxylamine (3v).**



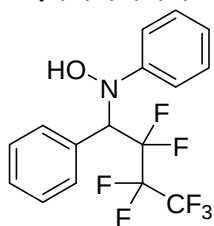
Yield 159 mg (78%). Colorless oil. Chromatography: hexanes/EtOAc, 10/1. R_f 0.36 (hexanes/EtOAc, 10/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.46–7.30 (m, 10H), 4.78 (s, 1H), 4.06 (d, J = 13.2 Hz, 1H), 3.79 (d, J = 13.2 Hz, 1H), 3.55 (m, 1H), 2.96 (m, 2H), 2.41 (m, 2H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 141.1, 137.2, 129.3, 128.8, 128.7, 128.5, 127.7, 126.5, 64.2 (dd, J = 25.9, 19.7 Hz), 61.9, 33.9 (d, J = 3.1 Hz), 23.8.

^{19}F NMR (282 MHz, CDCl_3) δ : –81.4 (dd, J = 13.2, 8.2 Hz, 3F), –113.0 (dm, J = 286.3 Hz, 1F), –112.4 (dm, J = 286.3 Hz, 1F), –124.3 (ddd, J = 289.9, 13.6, 9.1 Hz, 1F), –128.0 (dd, J = 289.9, 14.5 Hz, 1F).

HRMS (ESI): calcd for $\text{C}_{19}\text{H}_{18}\text{F}_7\text{NONa}$ ($\text{M}+\text{Na}$) 432.1169; found 432.1161.

***N*-(2,2,3,3,4,4,4-heptafluoro-1-phenylbutyl)-*N*-phenylhydroxylamine (3w).**

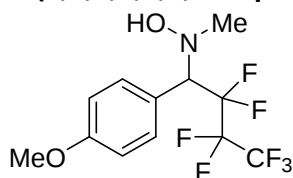
Yield 133 mg (72%). Colorless crystals. Mp 56–58 °C. Chromatography: hexanes/EtOAc, 10/1. R_f 0.38 (hexanes/EtOAc, 10/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.47–7.26 (m, 7H), 7.14–7.03 (m, 3H), 5.26 (s, 1H), 5.07 (dd, J = 20.7, 9.3 Hz, 1H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 150.3, 131.5, 129.3, 128.9, 128.5, 128.1, 123.6, 117.9, 70.8 (dd, J = 27.7, 18.4 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : –81.4 (t, J = 10.7 Hz, 3F), –112.2 (dm, J = 285.3, 1F), –118.2 (dm, J = 285.3 Hz, 1F), –125.2 (ddd, J = 289.9, 13.6, 6.5 Hz, 1F), –127.2 (dd, J = 289.9, 14.5 Hz, 1F).

HRMS (ESI): calcd for $\text{C}_{16}\text{H}_{12}\text{F}_7\text{NONa}$ ($\text{M}+\text{H}$) 390.0699; found 390.0704.

***N*-(2,2,3,3,4,4,4-Heptafluoro-1-(4-methoxyphenyl)butyl)-*N*-methylhydroxylamine (3x)**

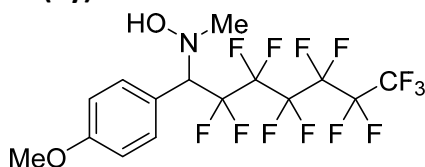
Yield 146 mg (87%). Colorless crystals. Mp 35–37 °C. Chromatography: hexanes/EtOAc, 5/1. R_f 0.26 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.44 (d, J = 8.6 Hz, 2H), 6.94 (d, J = 8.6 Hz, 2H), 5.67 (s, 1H), 4.20 (dd, J = 17.2, 12.3 Hz, 1H), 3.83 (s, 3H), 2.53 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 160.5, 133.1, 120.8, 113.8, 70.4 (dd, J = 24.6, 18.5 Hz), 55.3, 45.9.

^{19}F NMR (282 MHz, CDCl_3) δ : –81.6 (t, J = 10.7 Hz, 3F), –113.9 (d, J = 282.7 Hz, 1F), –118.5 (d, J = 282.7 Hz, 1F), –126.2 (dd, J = 11.4, 6.4 Hz, 2F).

HRMS (ESI): calcd for $\text{C}_{12}\text{H}_{10}\text{F}_7\text{NO}_2\text{Na}$ ($\text{M}+\text{H}$) 356.0492; found 356.0495.

***N*-Methyl-*N*-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-1-(4-methoxyphenyl)heptyl)hydroxylamine (3y)**

Yield 209 mg (86%). Colorless crystals. Mp 63–66 °C. Chromatography: hexanes/EtOAc, 5/1. R_f 0.33 (hexanes/EtOAc, 5/1).

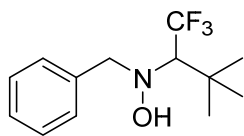
^1H NMR (300 MHz, CDCl_3) δ : 7.45 (d, J = 8.7 Hz, 2H), 6.94 (d, J = 8.7 Hz, 2H), 5.67 (br. s, 1H), 4.22 (dd, J = 17.4, 12.4 Hz, 1H), 3.83 (s, 3H), 2.53 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 160.5, 133.1, 120.8, 113.8, 70.6 (dd, J = 24.6, 18.3 Hz), 55.3, 45.9.

^{19}F NMR (282 MHz, CDCl_3) δ : –81.9 (t, J = 10.1 Hz, 3F), –113.4 (dm, J = 283.8 Hz, 1F), –117.5 (dm, J = 283.8 Hz, 1F), –121.8 (m, 2F), –122.8 (m, 2F), –123.7 (m, 2F), –127.2 (m, 2F).

HRMS (ESI): calcd for $C_{15}H_{13}F_{13}NO_2$ (M+H) 486.0733; found 486.0723.

***N*-Benzyl-*N*-(1,1,1-trifluoro-3,3-dimethylbutan-2-yl)hydroxylamine (3z).**



Yield 69 mg (53%). Colorless oil. Chromatography: hexanes/EtOAc, 10/1. R_f 0.32 (hexanes/EtOAc, 10/1).

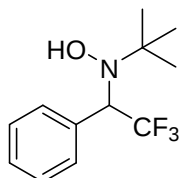
1H NMR (300 MHz, $CDCl_3$) δ : 7.41–7.31 (m, 5H), 4.71 (br. s, 1H), 4.38 (d, J = 13.4 Hz, 1H), 3.99 (d, J = 13.4 Hz, 1H), 3.05 (q, J = 9.2 Hz, 1H), 1.13 (s, 9H).

^{13}C NMR (75.5 MHz, $CDCl_3$) δ : 138.3, 129.4, 128.6, 127.7, 127.1 (q, J = 291.4 Hz), 73.7 (q, J = 22.4 Hz), 64.3, 35.0, 28.3.

^{19}F NMR (282 MHz, $CDCl_3$) δ : –59.7 (d, J = 9.2 Hz).

HRMS (ESI): calcd for $C_{13}H_{19}F_3NO$ (M+H) 262.1413; found 262.1419.

***N*-(*tert*-Butyl)-*N*-(2,2,2-trifluoro-1-phenylethyl)hydroxylamine (3 π).**



Yield 49 mg (40%). Colorless oil. Chromatography: hexanes/EtOAc, 8/1. R_f 0.20 (hexanes/EtOAc, 10/1).

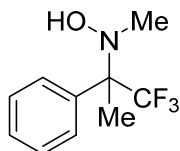
1H NMR (300 MHz, $CDCl_3$) δ : 7.64–7.58 (m, 2H), 7.41–7.35 (m, 3H), 4.72 (br s, 1H), 4.52 (q, J = 8.6 Hz, 1H), 1.07 (s, 9H).

^{13}C NMR (75.5 MHz, $CDCl_3$) δ : 132.6, 131.4, 128.5, 127.8, 125.3 (q, J = 281.9 Hz), 65.1 (q, J = 28.1 Hz), 60.1, 26.5.

^{19}F NMR (282 MHz, $CDCl_3$) δ : –71.5 (d, J = 8.6 Hz).

HRMS (ESI): calcd for $C_{12}H_{17}F_3NO$ (M+H) 248.1257; found 248.1255.

***N*-methyl-*N*-(1,1,1-trifluoro-2-phenylpropan-2-yl)hydroxylamine (3 σ).**



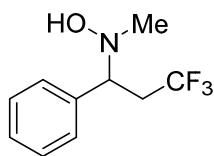
Yield 57 mg (52%). Colorless crystals. Mp 73–74 °C. Chromatography: hexanes/EtOAc, 5/1. R_f 0.34 (hexanes/EtOAc, 5/1).

1H NMR (300 MHz, $CDCl_3$) δ : 7.63–7.58 (m, 2H), 7.42–7.34 (m, 3H), 5.46 (s, 1H), 2.47 (s, 3H), 1.75 (s, 3H).

^{13}C NMR (75.5 MHz, $CDCl_3$) δ : 137.6, 128.8, 128.5, 128.0, 126.4 (q, J = 285.8 Hz), 70.7 (q, J = 24.5 Hz), 41.2, 10.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ : –73.4.

HRMS (ESI): calcd for $C_{10}H_{13}F_3NO$ (M+H) 220.0944; found 220.0953.

***N*-Methyl-*N*-(3,3,3-trifluoro-1-phenylpropyl)hydroxylamine (6a).**

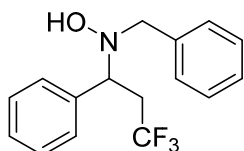
Yield 90 mg (82%). Colorless crystals. Mp 76–79 °C. Chromatography: hexanes/EtOAc, 3/1. R_f 0.19 (hexanes/EtOAc, 4/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.42–7.31 (s, 5H), 3.86 (dd, J = 9.3, 4.1 Hz, 1H), 3.21–3.03 (m, 1H), 2.75–2.61 (m, 1H), 2.48 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 137.7, 128.8, 128.8, 128.6, 126.4 (q, J = 276.8 Hz), 68.0, 46.1, 37.6 (q, J = 27.2 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : -63.8 (t, J = 10.4 Hz).

HRMS (ESI): calcd for $\text{C}_{10}\text{H}_{13}\text{F}_3\text{NO}$ ($\text{M}+\text{H}$) 220.0944; found 220.0946.

***N*-Benzyl-*N*-(3,3,3-trifluoro-1-phenylpropyl)hydroxylamine (6b).**

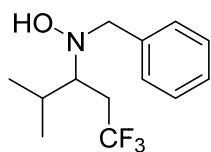
Yield 117 mg (79%). Colorless oil. Chromatography: hexanes/EtOAc, 8/1. R_f 0.35 (hexanes/EtOAc, 8/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.53–7.30 (m, 10H), 5.41 (s, 1H), 4.10 (dd, J = 8.4, 5.1 Hz, 1H), 3.70 (d, J = 13.2 Hz, 1H), 3.58 (d, J = 13.2 Hz, 1H), 3.23–3.05 (m, 1H), 2.73–2.55 (m, 1H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 137.8, 137.6, 129.5, 129.0, 128.7, 128.5, 128.4, 127.6, 126.2 (q, J = 227.2 Hz), 65.7, 61.5, 37.6 (q, J = 26.9 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : -63.5 (t, J = 10.5 Hz).

HRMS (ESI): calcd for $\text{C}_{16}\text{H}_{17}\text{F}_3\text{NO}$ ($\text{M}+\text{H}$) 296.1257; found 296.1257.

***N*-Benzyl-*N*-(1,1,1-trifluoro-4-methylpentan-3-yl)hydroxylamine (6c).**

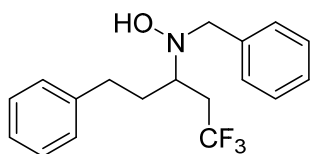
Yield 98 mg (75%). Colorless crystals. Mp 57–59 °C. Chromatography: hexanes/EtOAc, 10/1. R_f 0.52 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.41–7.28 (m, 5H), 4.41 (br s, 1H), 3.87 (q, J = 12.6 Hz, 2H), 2.90–2.71 (m, 2H), 2.30–2.11 (m, 2H), 2.00 (sextet, J = 6.8 Hz, 1H), 1.06 (d, J = 6.8 Hz, 3H), 1.02 (d, J = 6.8 Hz, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 138.2, 129.3, 128.5, 127.5 (q, J = 276.0 Hz), 127.5, 65.3, 62.0, 31.2, 30.7 (q, J = 27.9 Hz), 20.1, 19.6.

^{19}F NMR (282 MHz, CDCl_3) δ : -63.9 (t, J = 11.5 Hz).

HRMS (ESI): calcd for $\text{C}_{13}\text{H}_{19}\text{F}_3\text{NO}$ ($\text{M}+\text{H}$) 262.1413; found 262.1419.

***N*-Benzyl-*N*-(1,1,1-trifluoro-5-phenylpentan-3-yl)hydroxylamine (6d).**

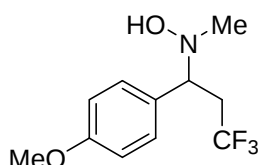
Yield 100 mg (62%). Colorless oil. Chromatography: hexanes/EtOAc, 10/1. R_f 0.28 (hexanes/EtOAc, 10/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.45–7.25 (m, 10H), 5.18 (br s, 1H), 3.88 (q, J = 12.9 Hz, 2H), 3.17–3.08 (m, 1H), 3.93–3.73 (m, 3H), 2.35–2.10 (s, 2H), 2.05–1.92 (s, 1H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 141.7, 137.6, 129.5, 128.6, 128.5, 127.6, 127.2 (q, J = 276.6 Hz), 126.1, 60.5, 59.5 (q, J = 2.1 Hz), 33.3 (q, J = 27.4 Hz), 33.3, 32.6.

^{19}F NMR (282 MHz, CDCl_3) δ : –64.0 (t, J = 11.5 Hz),

HRMS (ESI): calcd for $\text{C}_{18}\text{H}_{21}\text{F}_3\text{NO}$ ($M+H$) 324.1570; found 324.1568.

***N*-Methyl-*N*-(3,3,3-trifluoro-1-(4-methoxyphenyl)propyl)hydroxylamine (6e).**

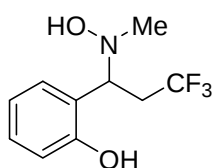
Yield 70 mg (56%). Colorless crystals. Mp 101–102 °C. Chromatography: hexanes/EtOAc, 3/1. R_f 0.25 (hexanes/EtOAc, 3/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.22 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 3.80 (s, 4H), 3.07 (m, 1H), 2.61 (m, 1H), 2.45 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 159.7, 129.9, 129.6, 126.4 (q, J = 276.6 Hz), 114.1, 67.2, 55.3, 45.9, 37.4 (q, J = 27.1 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : –63.7 (t, J = 10.2 Hz).

HRMS (ESI): calcd for $\text{C}_{11}\text{H}_{15}\text{F}_3\text{NO}_2$ ($M+H$) 250.1049; found 250.1052.

2-(3,3,3-trifluoro-1-(hydroxy(methyl)amino)propyl)phenol (6f)

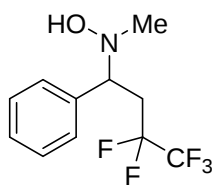
Yield 86 mg (73%). Yellow oil. Chromatography: hexanes/EtOAc, 2/1. R_f 0.34 (hexanes/EtOAc, 2/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.61 (br. s, 2H), 7.33–7.27 (m, 1H), 7.13 (d, J = 7.4 Hz, 1H), 6.98–6.91 (m, 2H), 4.04 (d, J = 7.0 Hz, 1H), 3.23–3.06 (m, 1H), 2.80–2.71 (m, 1H), 2.71 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 154.8, 130.2, 130.0, 126.1 (q, J = 276.7 Hz), 123.7, 120.6, 117.4, 68.1, 46.0, 35.8 (q, J = 28.1 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : –63.7 (br s).

HRMS (ESI): calcd for $\text{C}_{10}\text{H}_{13}\text{F}_3\text{NO}_2$ ($M+H$) 236.0893; found 236.0890.

***N*-Methyl-*N*-(3,3,4,4,4-pentafluoro-1-phenylbutyl)hydroxylamine (6g).**

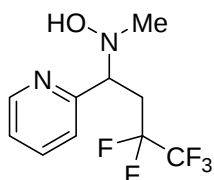
Yield 106 mg (78%). Colorless crystals. Mp 60–61 °C. Chromatography: hexanes/EtOAc, 4/1. R_f 0.20 (hexanes/EtOAc, 5/1).

^1H NMR (300 MHz, CDCl_3) δ : 7.41–7.31 (m, 5H), 7.04 (br s, 1H), 3.97 (dd, J = 9.0, 3.9 Hz, 1H), 3.12–2.97 (m, 1H), 2.72–2.54 (m, 1H), 2.47 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 138.1, 128.8, 128.8, 128.6, 119.2 (qt, J = 285.5, 36.0 Hz), 115.5 (tq, J = 253.7, 37.7 Hz), 66.8, 46.0, 34.0 (t, J = 20.1 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : –86.8 (s, 3F), –116.2 (br d, J = 266.6 Hz, 1F), –118.4 (ddd, J = 266.6, 27.7, 8.2 Hz, 1F).

HRMS (ESI): calcd for $\text{C}_{11}\text{H}_{13}\text{F}_5\text{NO}$ ($\text{M}+\text{H}$) 270.0912; found 270.0914.

***N*-Methyl-*N*-(3,3,4,4,4-pentafluoro-1-(pyridin-2-yl)butyl)hydroxylamine (6h).**

Yield 92 mg (68%). Colorless oil. Chromatography: hexanes/EtOAc, 1/1. R_f 0.30 (hexanes/EtOAc, 1/1).

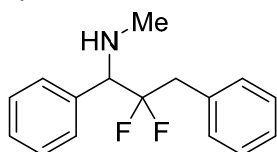
^1H NMR (300 MHz, CDCl_3) δ : 8.59 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 7.70 (td, J = 7.8, 1.8 Hz, 1H), 7.31 (dt, J = 7.8, 1.1 Hz, 1H), 7.25 (ddd, J = 7.8, 4.9, 1.2 Hz, 1H), 4.21–4.16 (m, 1H), 3.05–2.89 (m, 1H), 2.52 (s, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 158.2, 149.3, 137.0, 124.4, 123.3, 118.9 (qt, J = 285.3, 35.9 Hz), 115.7 (tq, J = 253.0, 37.8 Hz), 65.9, 45.3, 32.4 (t, J = 20.2 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : –86.8 (s, 3F), –116.4 (ddd, J = 265.0, 25.4, 13.2 Hz, 1F), –118.0 (ddd, J = 265.0, 25.3, 13.7 Hz, 1F).

HRMS (ESI): calcd for $\text{C}_{10}\text{H}_{12}\text{F}_5\text{N}_2\text{O}$ ($\text{M}+\text{H}$) 271.0864; found 271.0869.

Reduction of hydroxylamines 3a,b and 6b (General Procedure). Acetic acid (2 mL) and concentrated hydrochloric acid (80 μL) were added to a test tube containing fluorine-substituted hydroxylamine (0.50 mmol) and zinc dust (195 mg, 3.0 mmol), and the mixture was stirred for 24 h under air atmosphere at room temperature. The reaction mixture was poured portionwise into a solution of potassium hydroxide (1.9 g) in water (10 mL). The mixture was washed with MTBE (3 $\times$ 4 mL). The combined organic phases were washed with saturated aqueous NaHCO_3 solution, dried over Na_2SO_4 , concentrated, and the residue was dried under vacuum.

2,2-Difluoro-*N*-methyl-1,3-diphenylpropan-1-amine (7a).

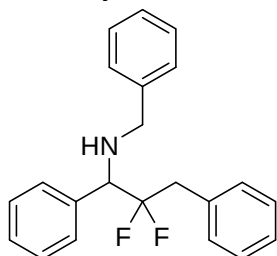
Yield 130 mg (100%). Colorless oil.

^1H NMR (300 MHz, CDCl_3) δ : 7.45–7.29 (m, 10H), 3.78 (dd, J = 14.1, 10.1 Hz, 1H), 3.51–3.33 (m, 1H), 3.11 (ddd, J = 26.5, 14.4, 12.1 Hz, 1H), 2.34 (s, 3H), 1.79 (s, 1H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 136.4 (t, J = 1.9 Hz), 133.2 (dd, J = 4.5, 2.9 Hz), 130.7, 129.0 (t, J = 1.3 Hz), 128.5, 128.3, 128.3, 127.2, 123.5 (t, J = 247.2 Hz), 68.0 (dd, J = 25.5, 24.4 Hz), 40.2 (t, J = 24.8 Hz), 34.3.

^{19}F NMR (282 MHz, CDCl_3) δ : -106.0 (dddd, J = 247.8, 26.6, 15.8, 10.7 Hz), -105.2 (ddt, J = 247.8, 20.4, 13.2 Hz)

HRMS (ESI): calcd for $\text{C}_{16}\text{H}_{18}\text{F}_2\text{N}$ ($\text{M}+\text{H}$) 262.1402; found 262.1396.

***N*-Benzyl-2,2-difluoro-1,3-diphenylpropan-1-amine (7b).**

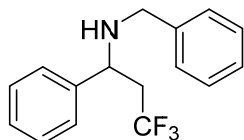
Yield 163 mg (97%). Colorless oil.

^1H NMR (300 MHz, CDCl_3) δ : 7.54–7.34 (m, 15H), 4.01 (dd, J = 16.5, 7.7 Hz, 1H), 3.86 (d, J = 13.1 Hz, 1H), 3.64 (d, J = 13.1 Hz, 1H), 3.54 (ddd, J = 31.2, 16.7, 14.5 Hz, 1H), 3.27 (ddd, J = 24.1, 14.6, 10.1 Hz, 1H), 2.18 (br s, 1H).

^{13}C NMR (75.5 MHz, CDCl_3) δ : 139.8, 136.5, 133.3 (dd, J = 5.6, 2.0 Hz), 130.7, 129.1 (t, J = 1.2 Hz), 128.5, 128.5, 128.4, 128.3, 127.3, 127.2, 123.5 (t, J = 247.0 Hz), 65.1 (dd, J = 26.8, 24.3 Hz), 51.1, 40.2 (dd, J = 25.2, 24.2 Hz).

^{19}F NMR (282 MHz, CDCl_3) δ : -104.0 (dddd, J = 248.6, 22.3, 16.5, 8.1 Hz, 1F), -106.5 (dddd, J = 248.6, 25.8, 15.7, 10.1 Hz, 1F).

HRMS (ESI): calcd for $\text{C}_{22}\text{H}_{22}\text{F}_2\text{N}$ ($\text{M}+\text{H}$) 338.1715; found 338.1709.

3,3,3-Trifluoro-*N*-methyl-1-phenylpropan-1-amine (7c).

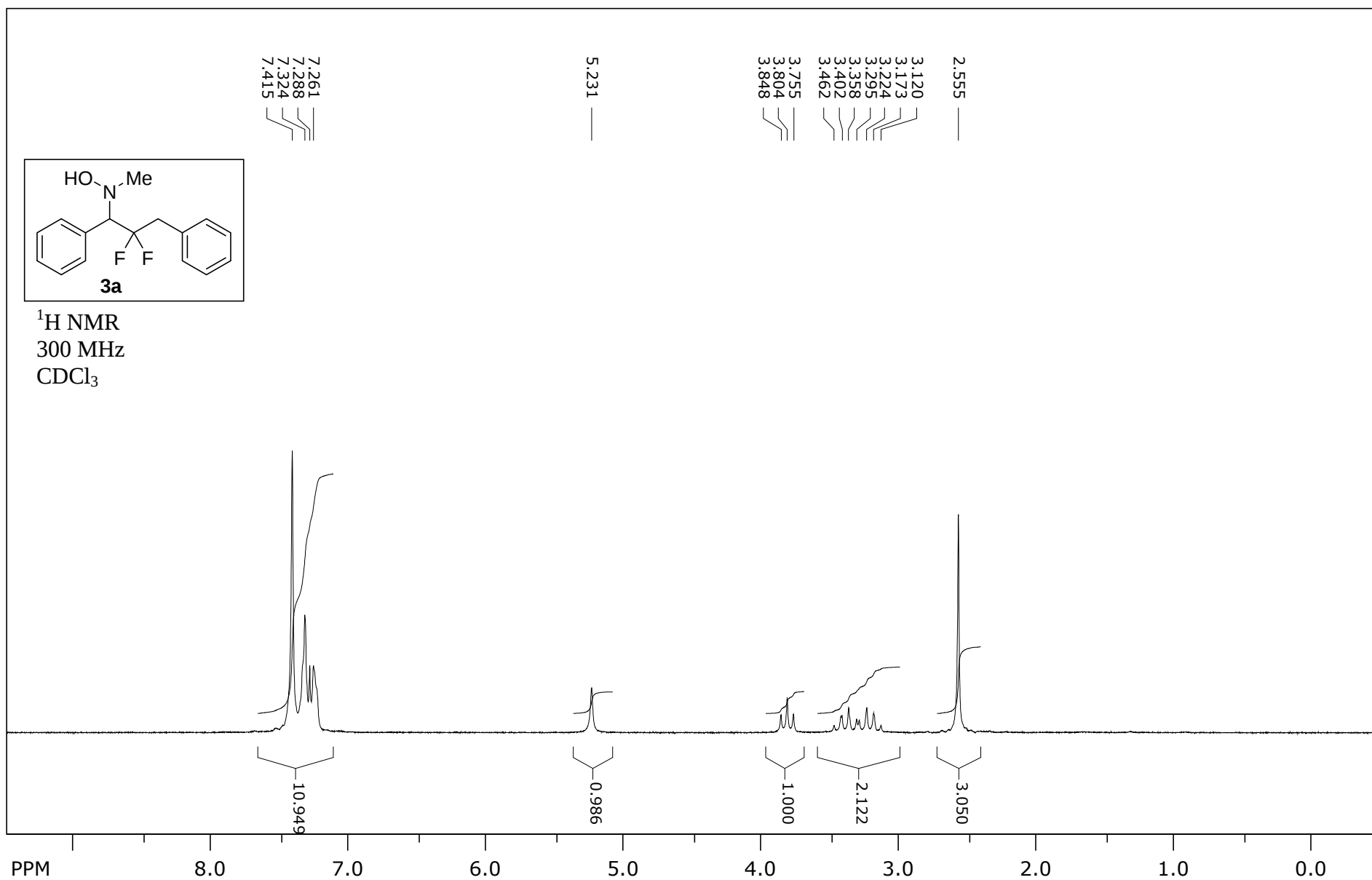
Yield 94 mg (93%). Colorless oil.

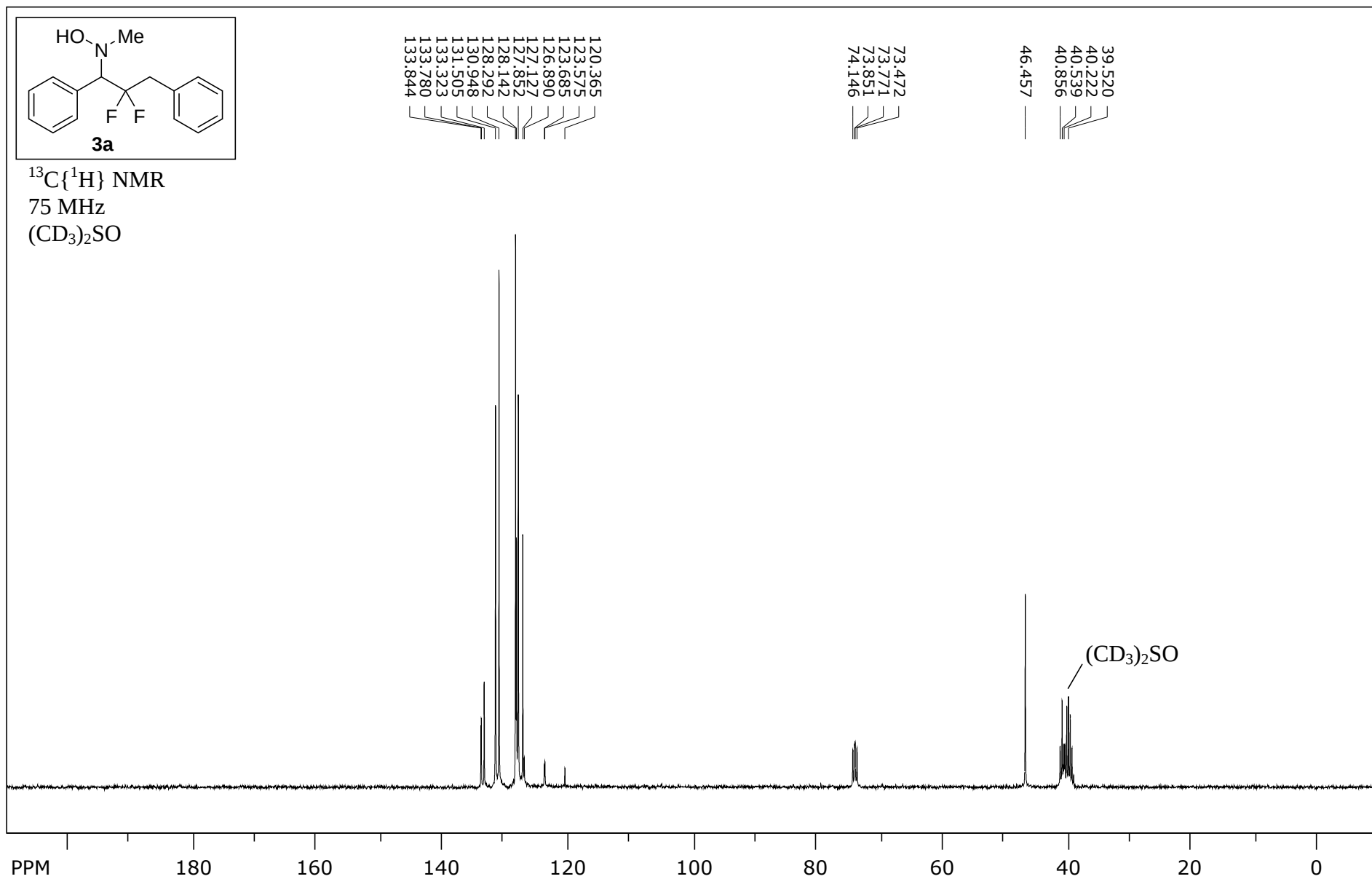
^1H NMR (300 MHz, CDCl_3) δ : 7.40–7.27 (m, 5H), 3.86 (dd, J = 7.4, 5.6 Hz, 1H), 2.62–2.37 (m, 2H), 2.27 (s, 3H), 1.66 (br. s, 1H).

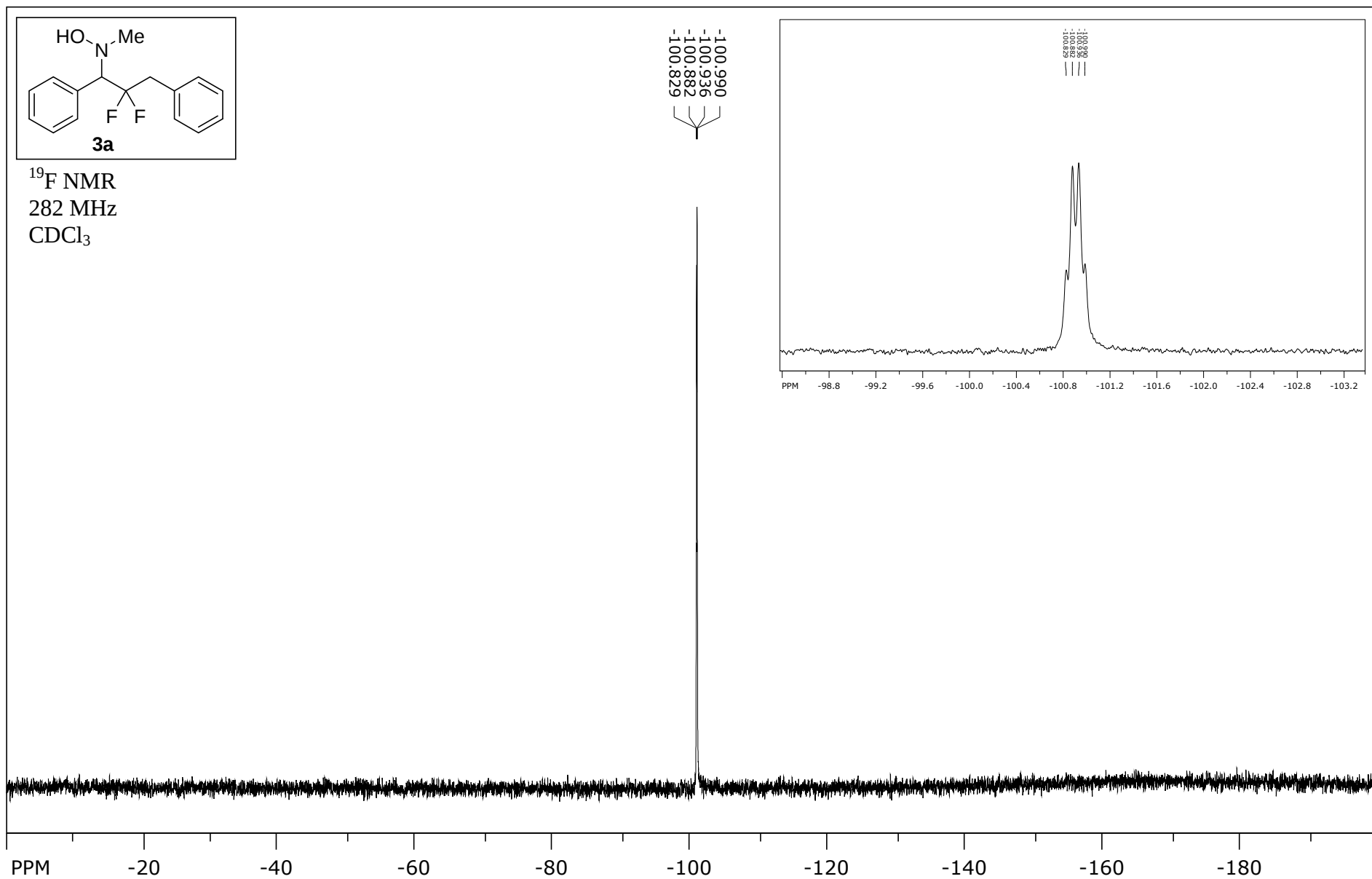
^{13}C NMR (75.5 MHz, CDCl_3) δ : 141.6, 128.9, 128.0, 127.2, 126.3 (q, J = 277.4 Hz), 59.5 (q, J = 2.8 Hz), 41.7 (q, J = 26.9 Hz), 34.1.

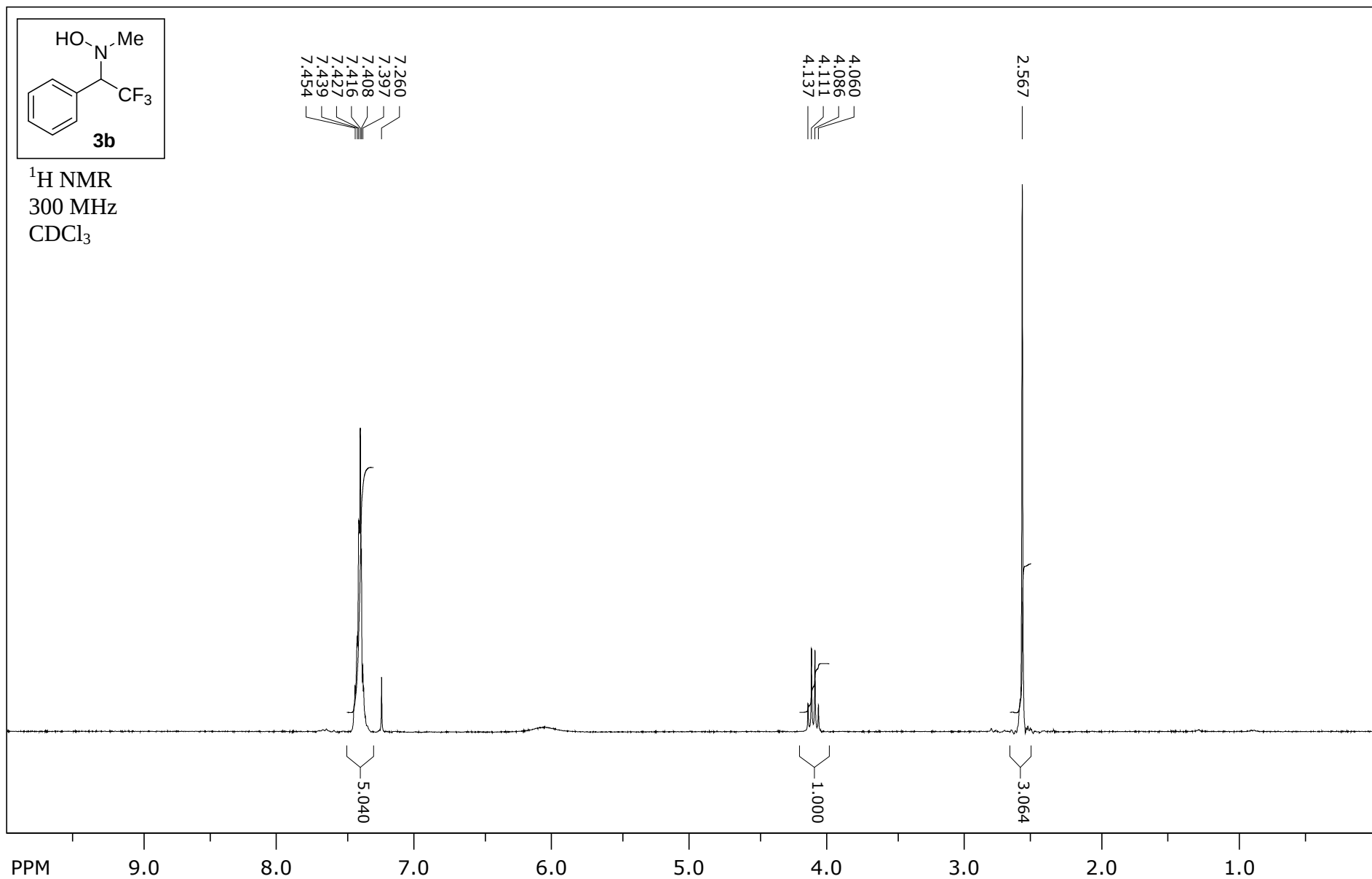
^{19}F NMR (282 MHz, CDCl_3) δ : -64.2 (t, J = 10.8 Hz).

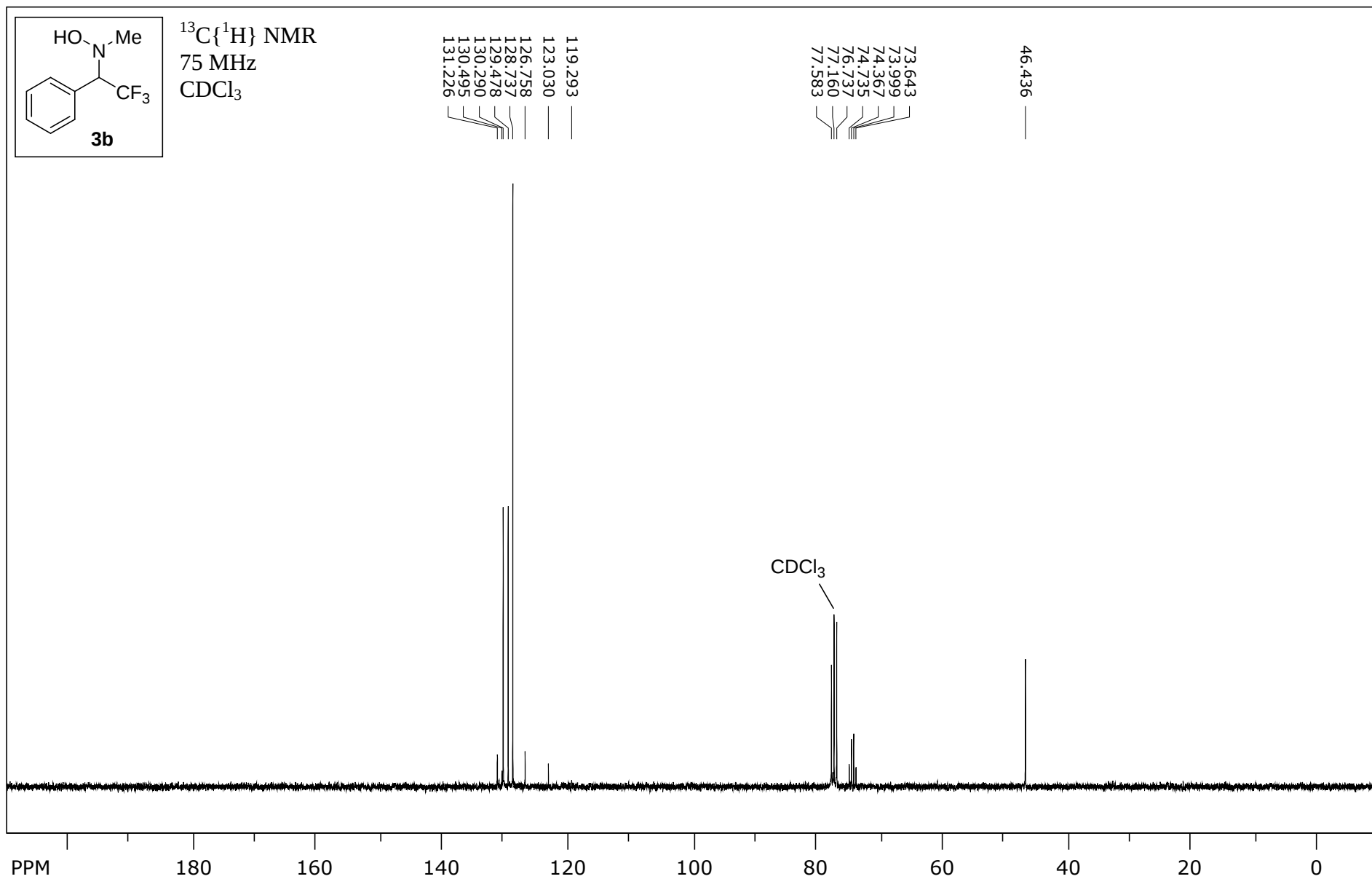
HRMS (ESI): calcd for $\text{C}_{10}\text{H}_{13}\text{F}_3\text{N}$ ($\text{M}+\text{H}$) 204.0995; found 204.0999.

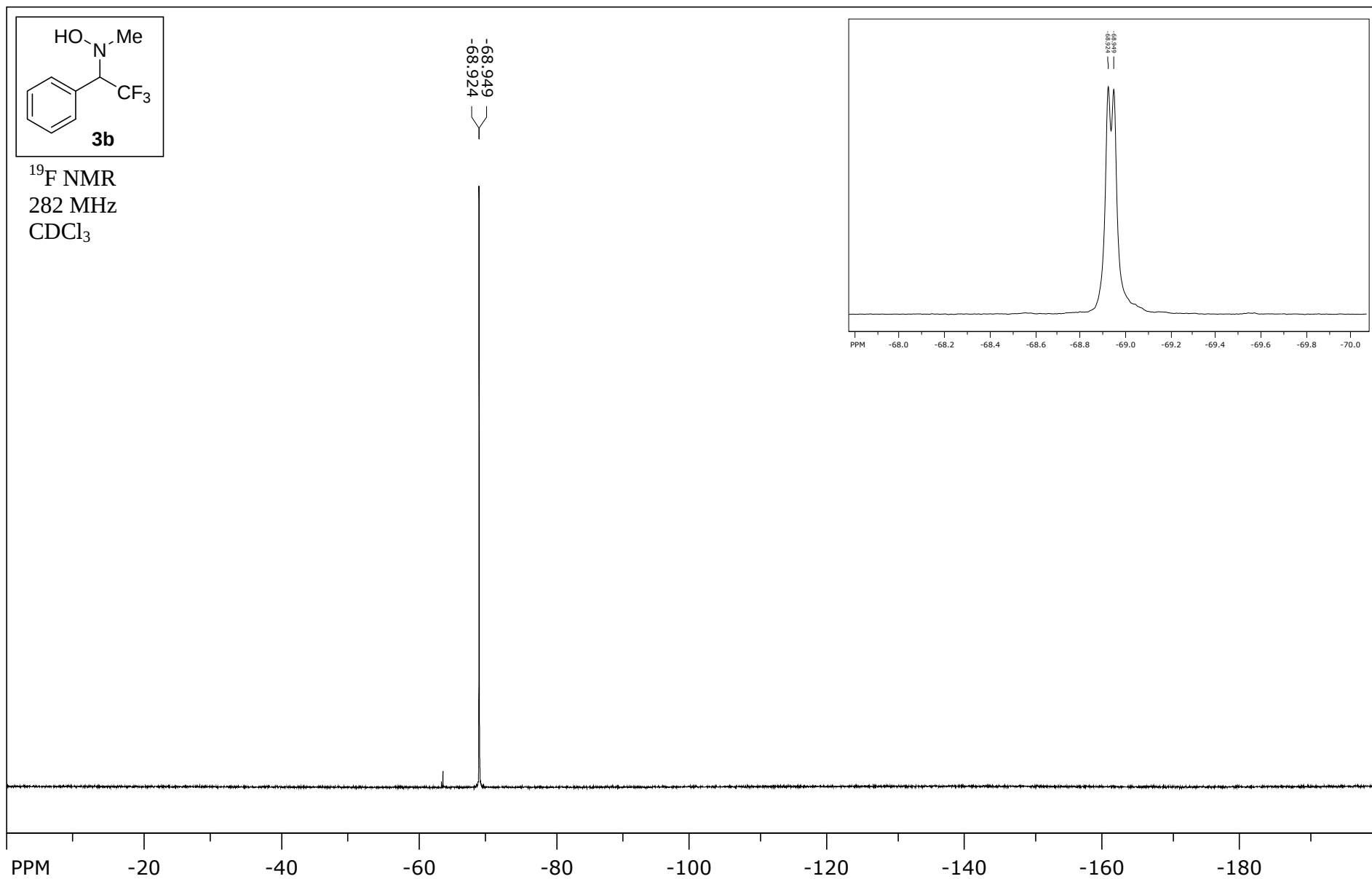


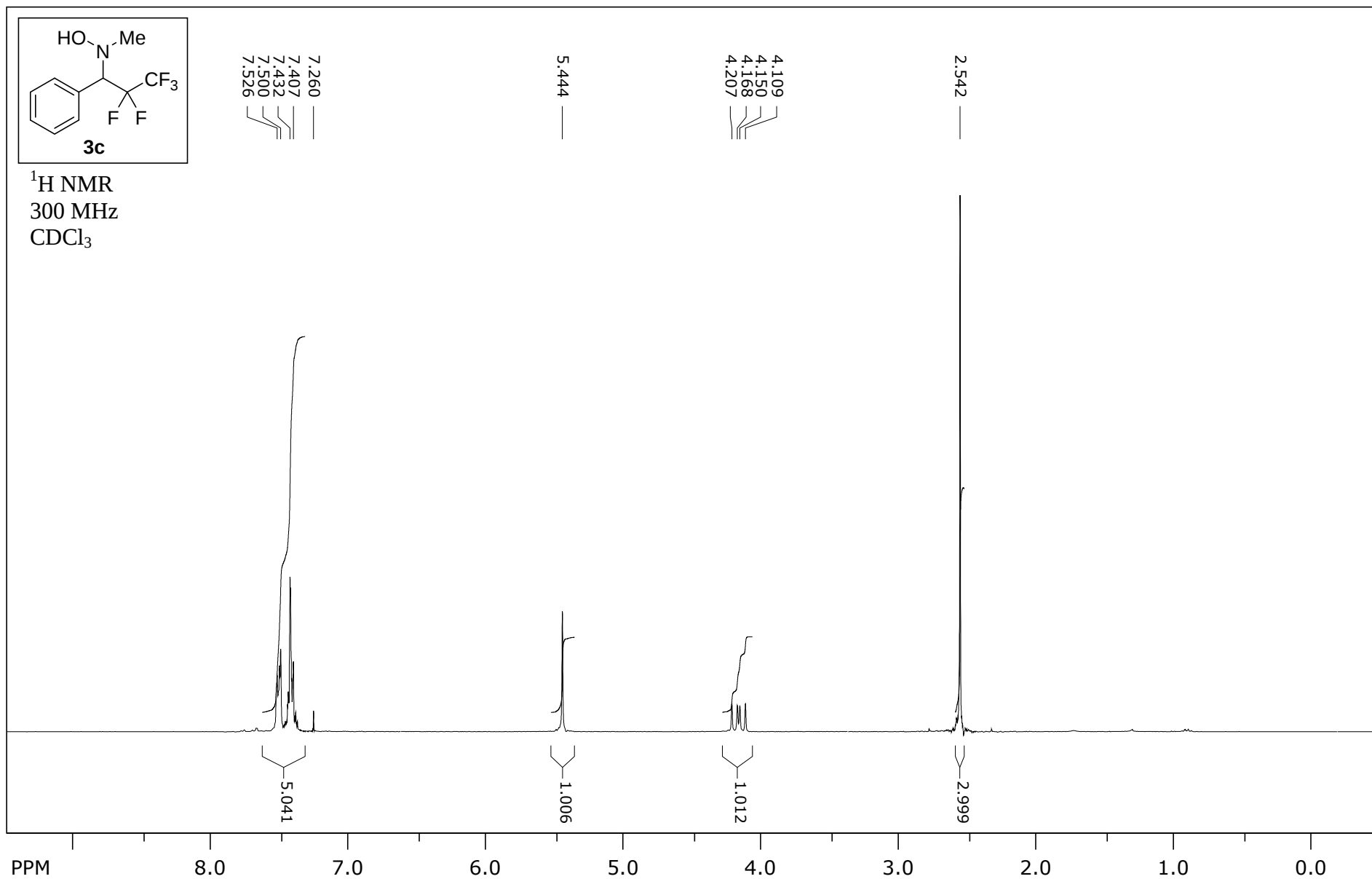


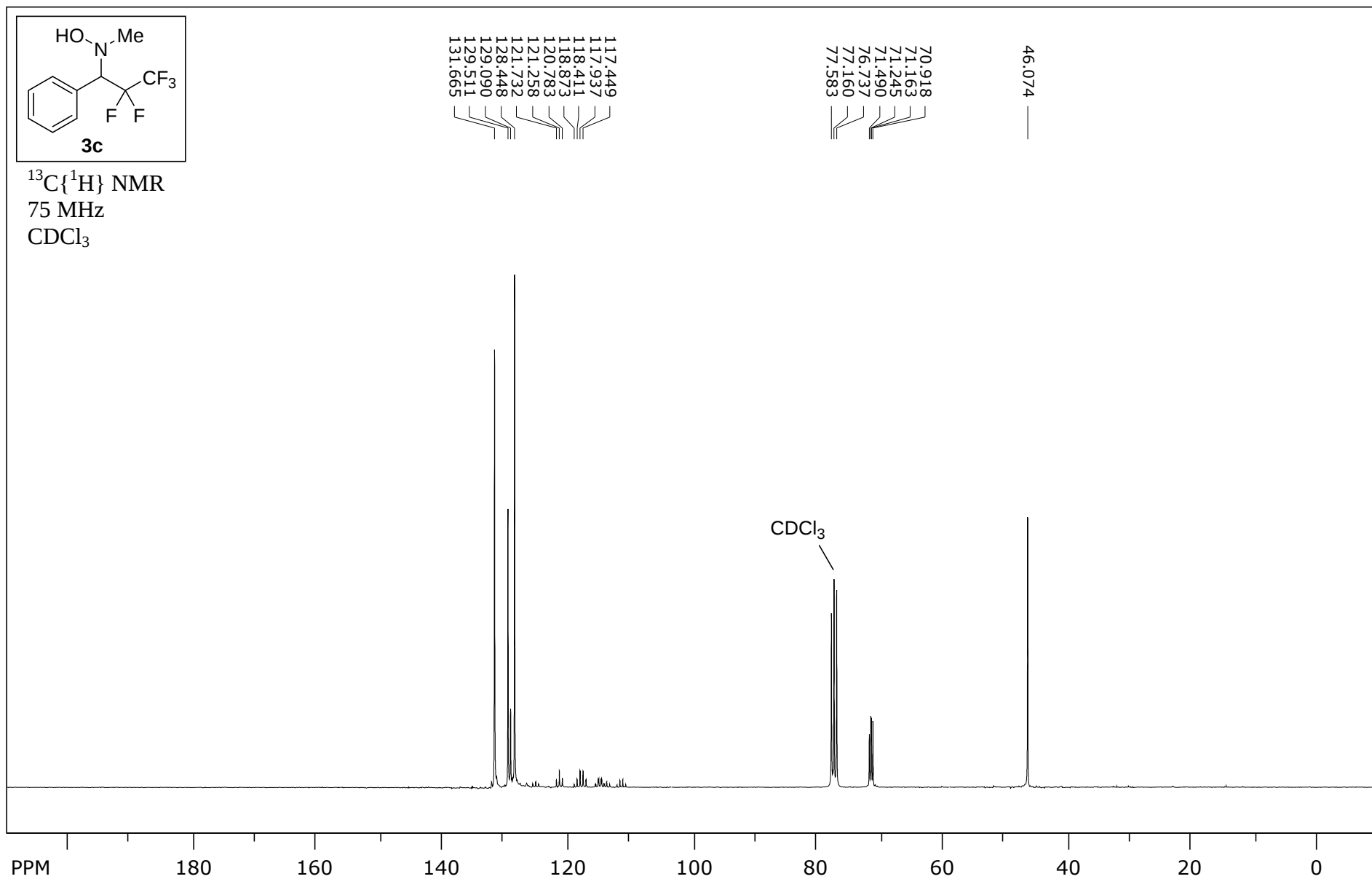


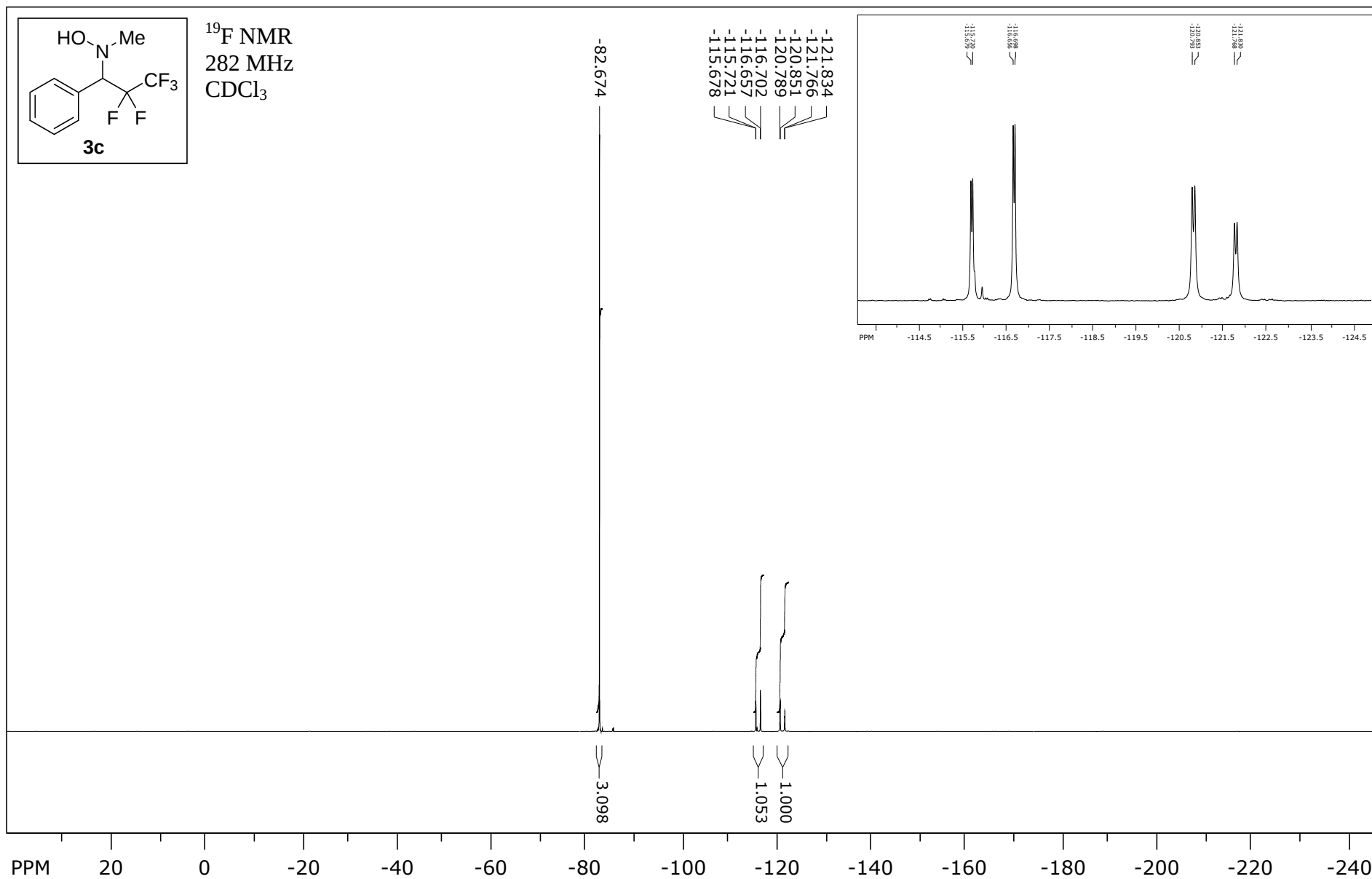


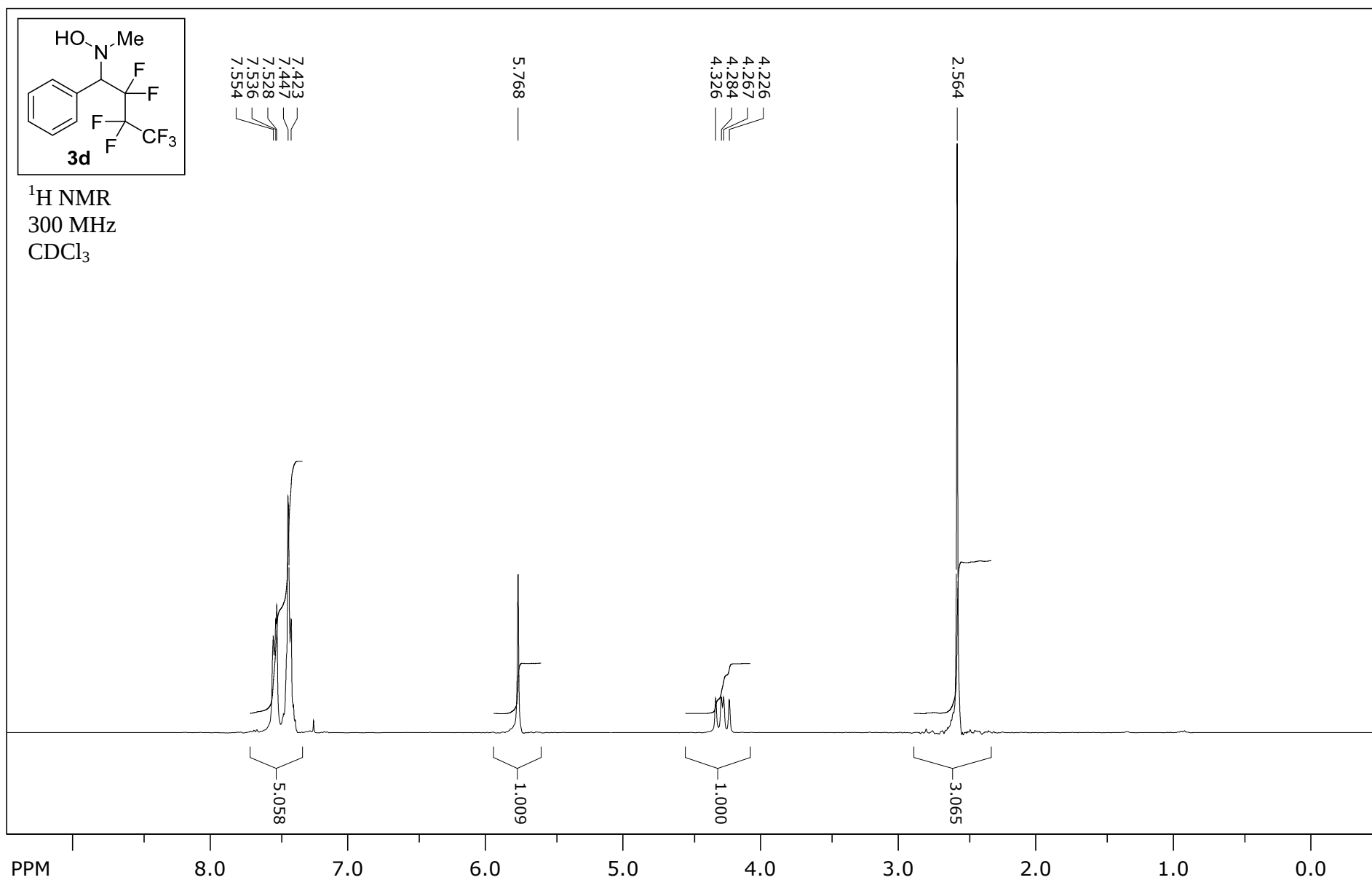


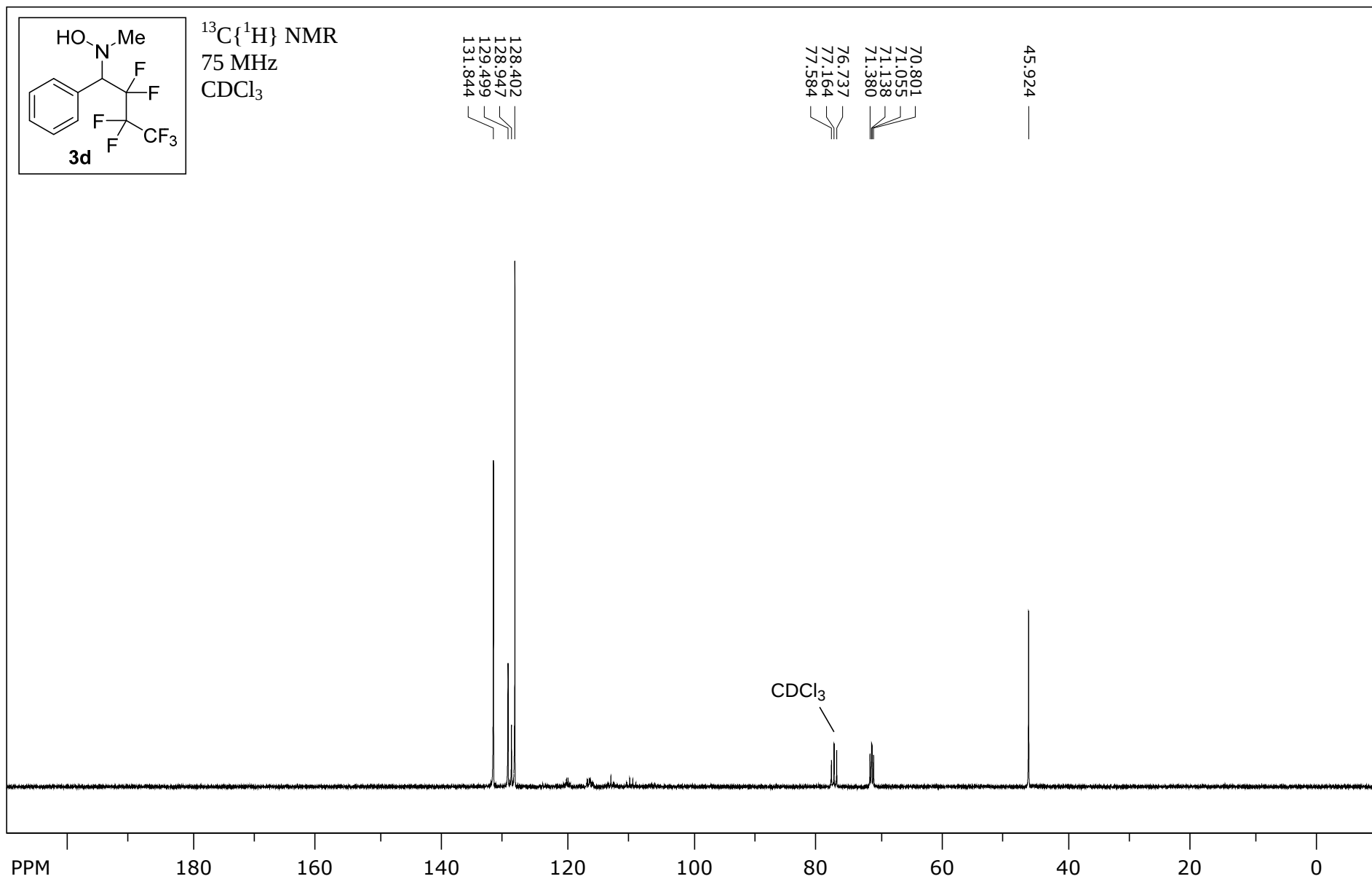


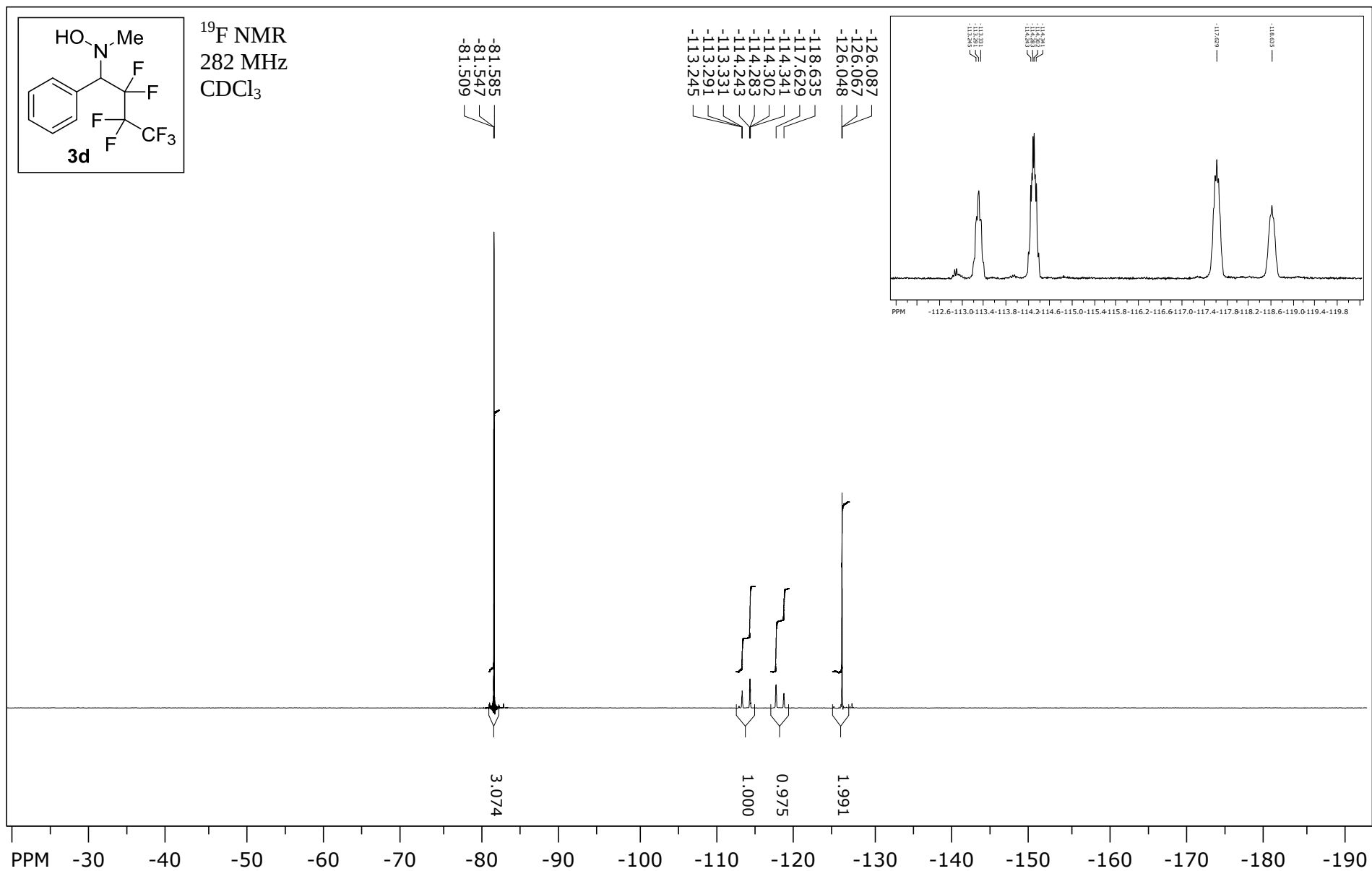


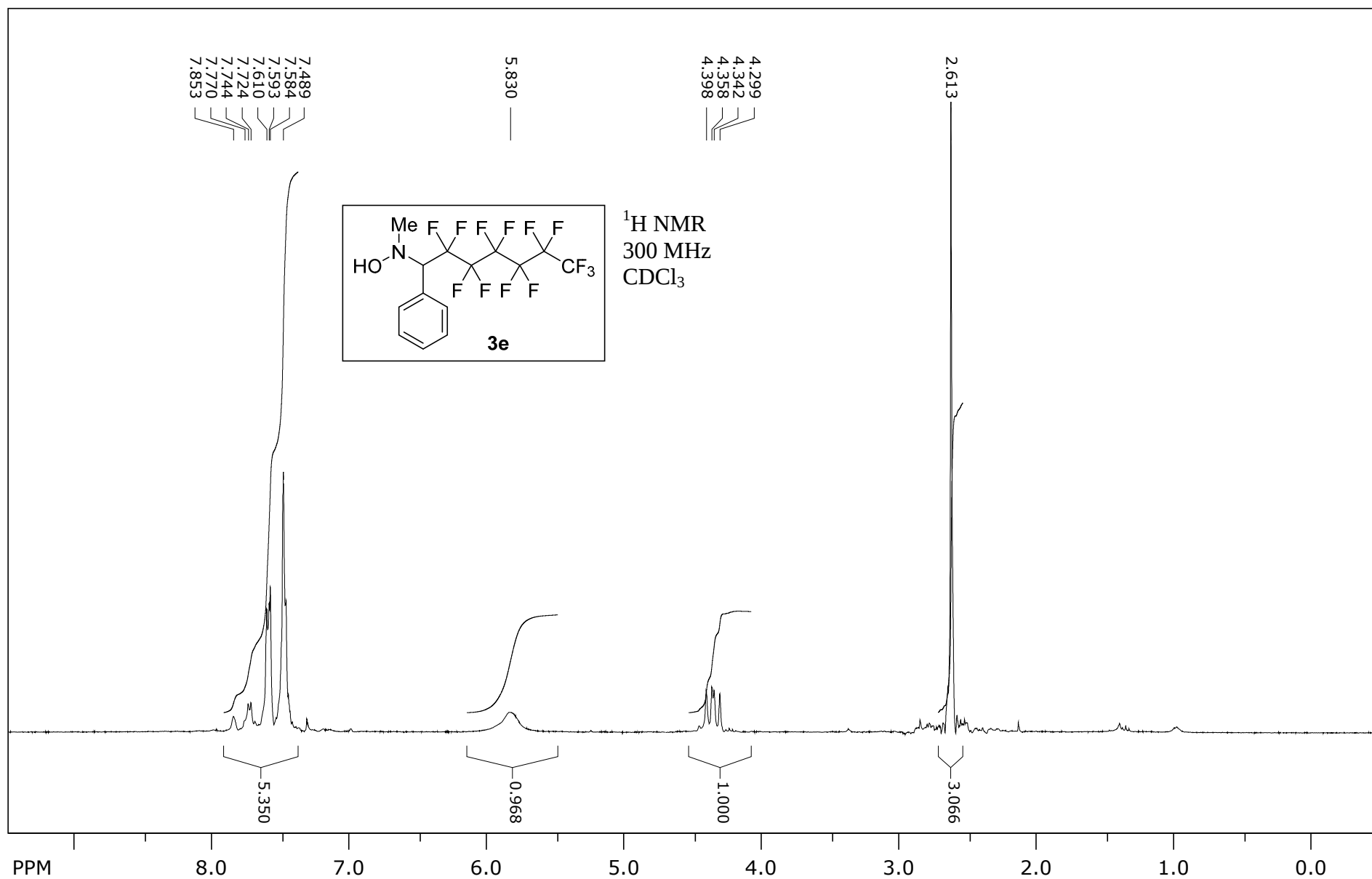


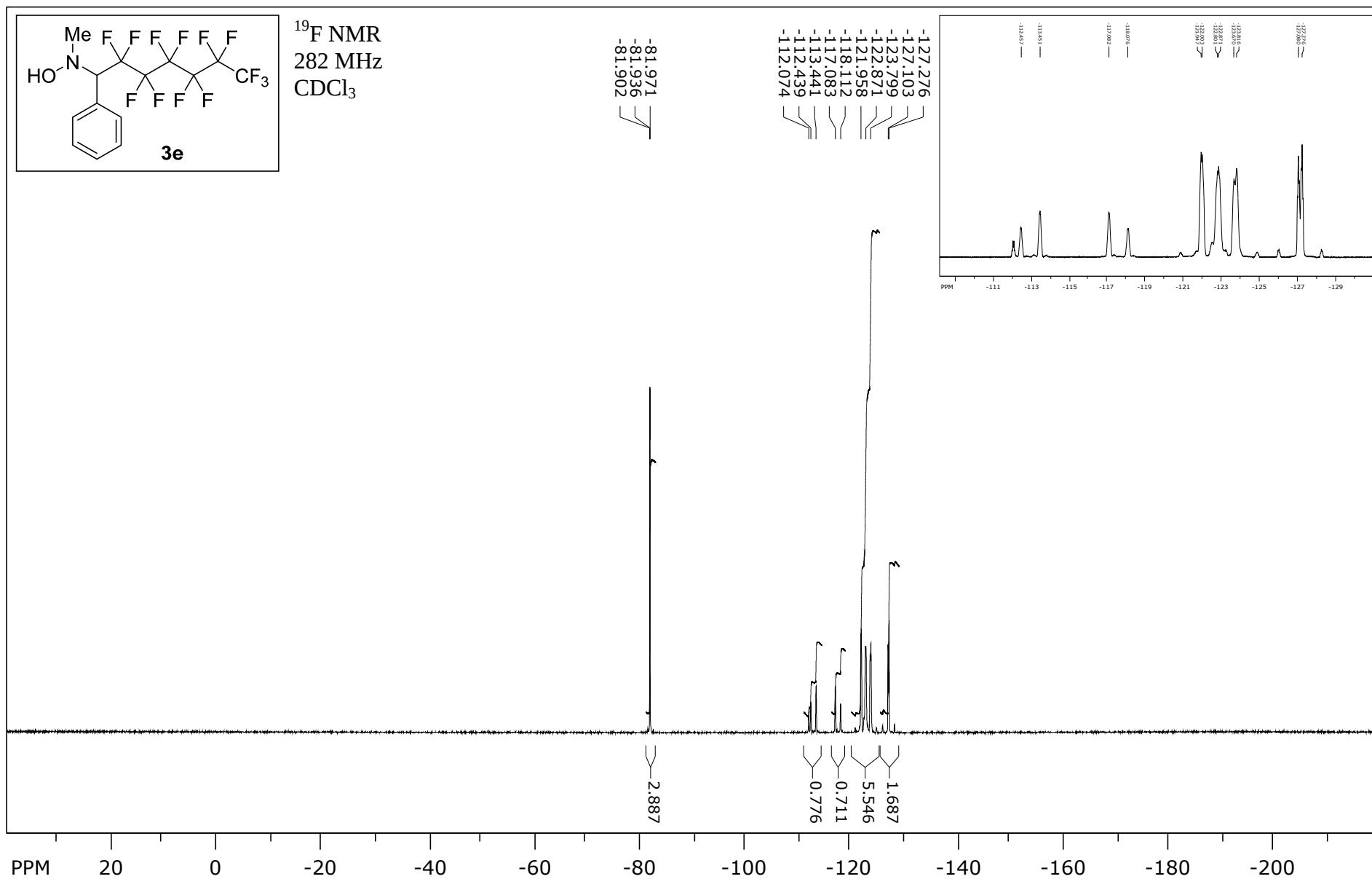


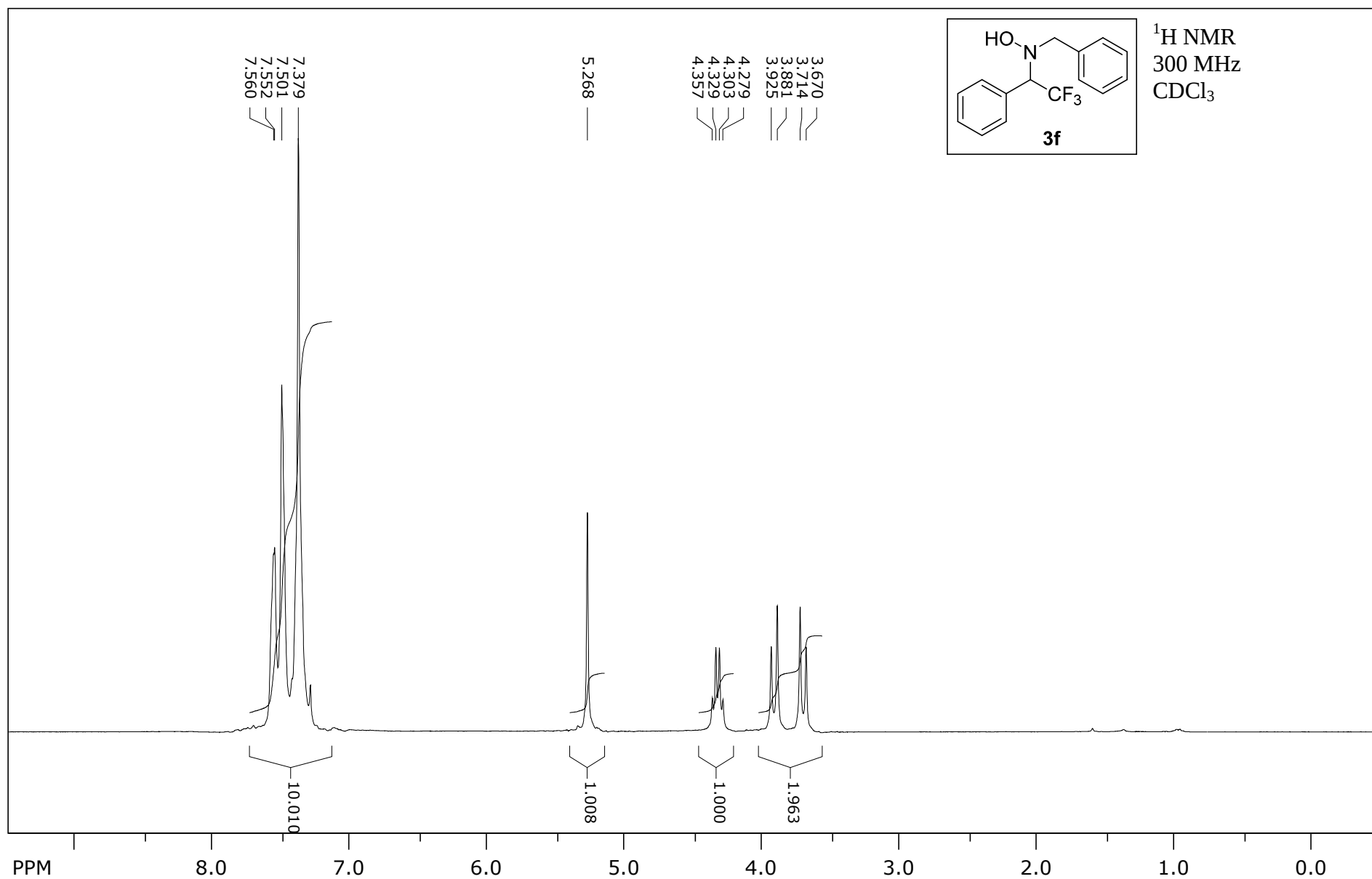


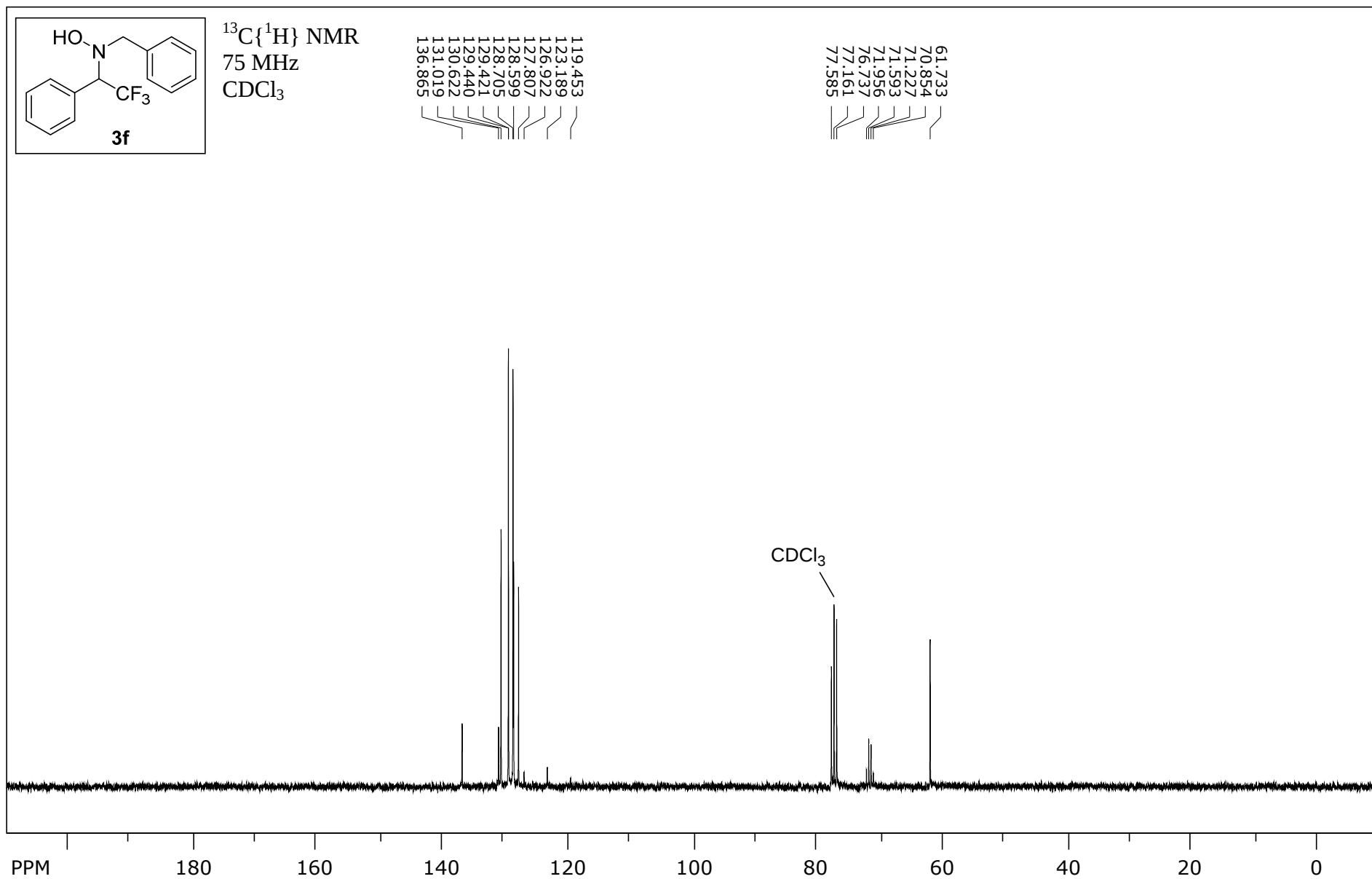


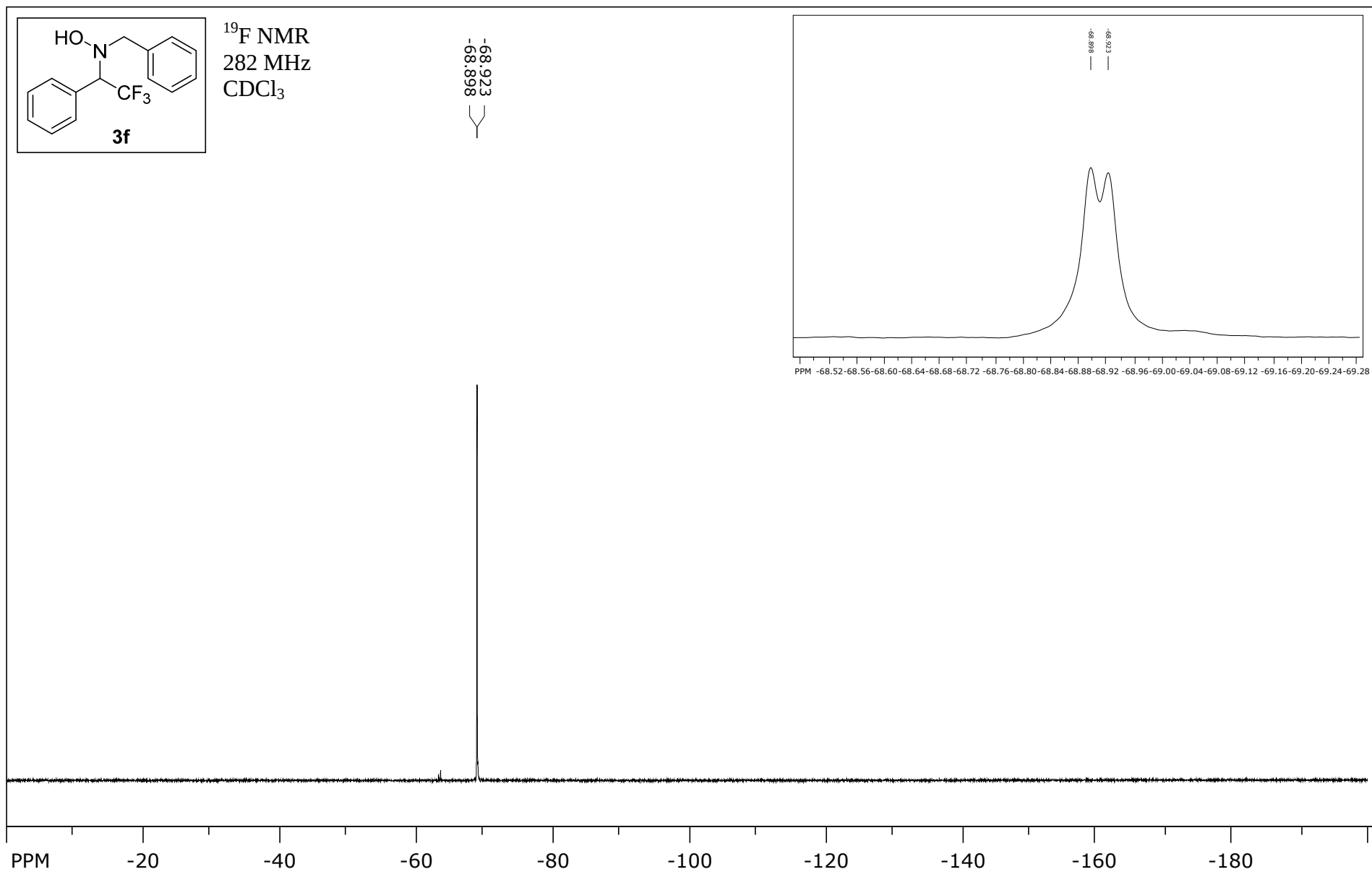


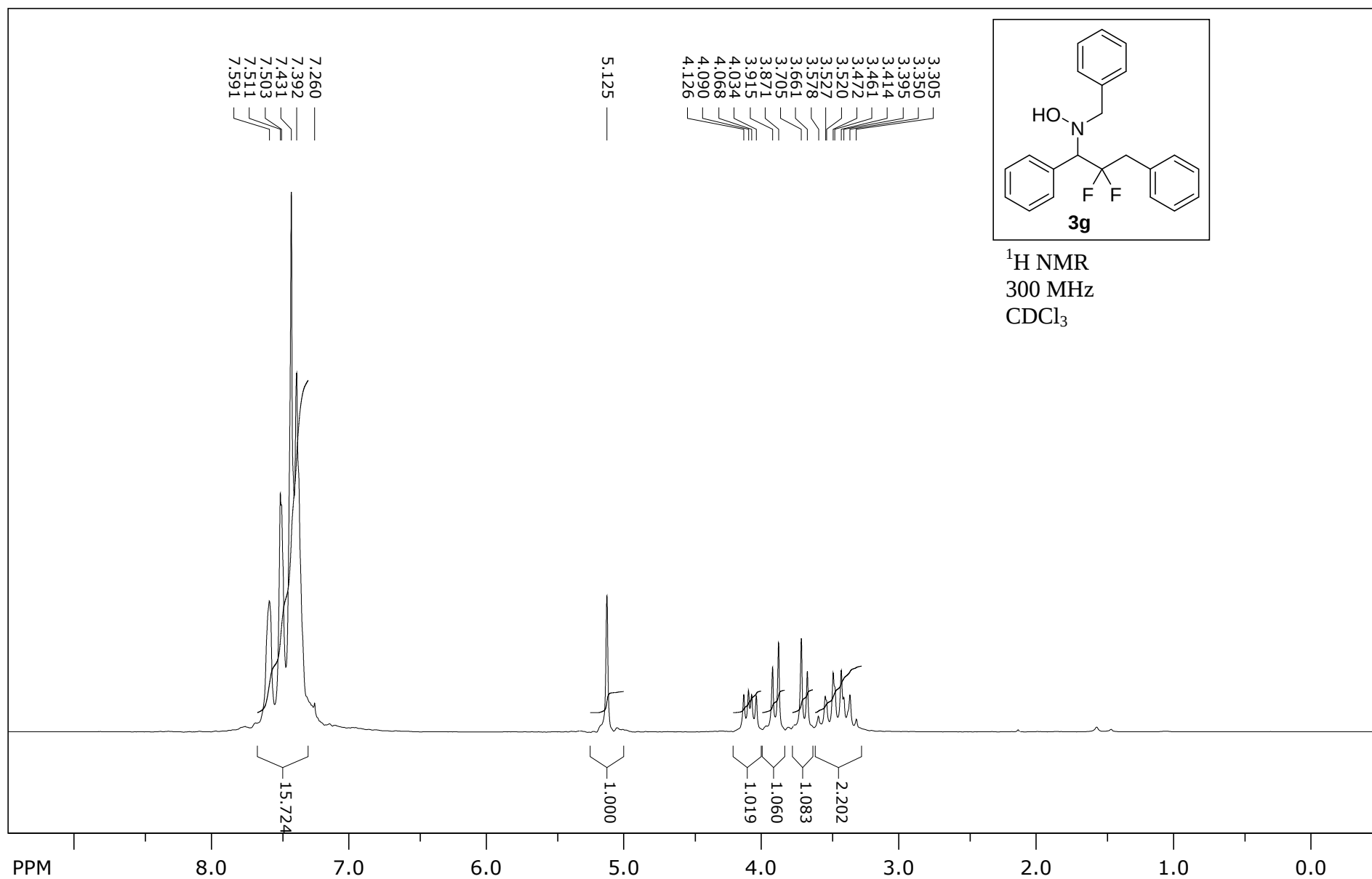


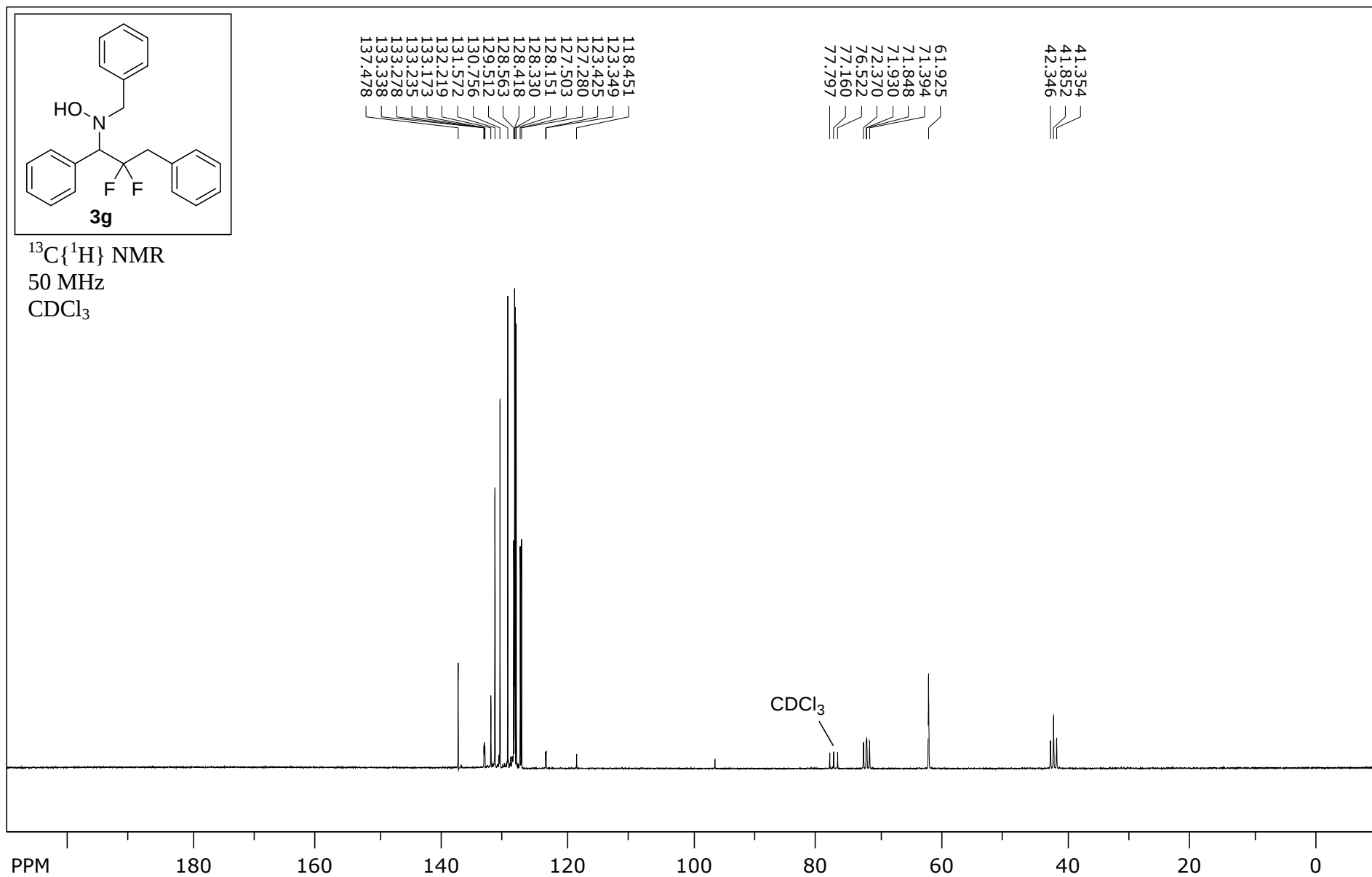


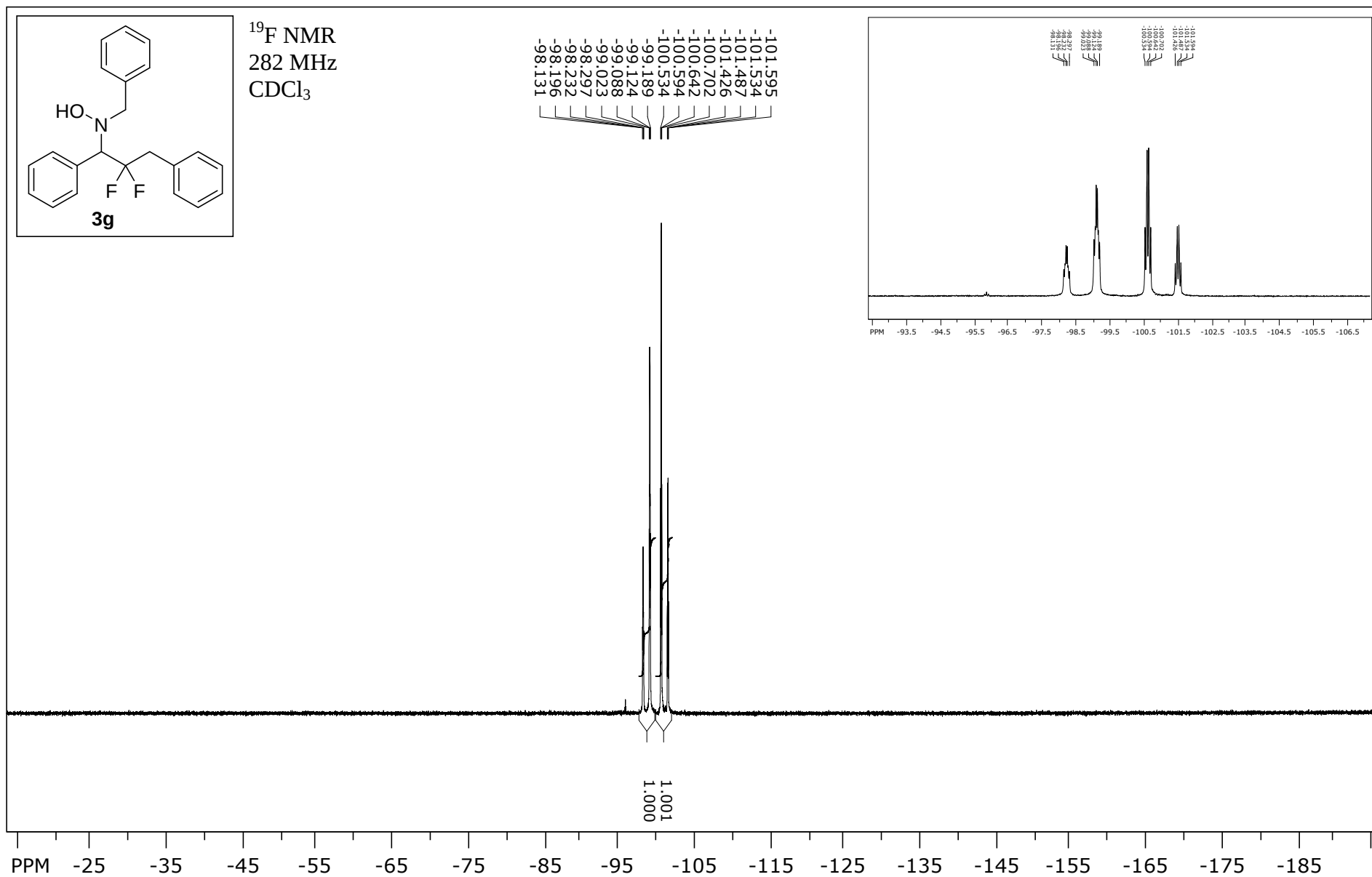


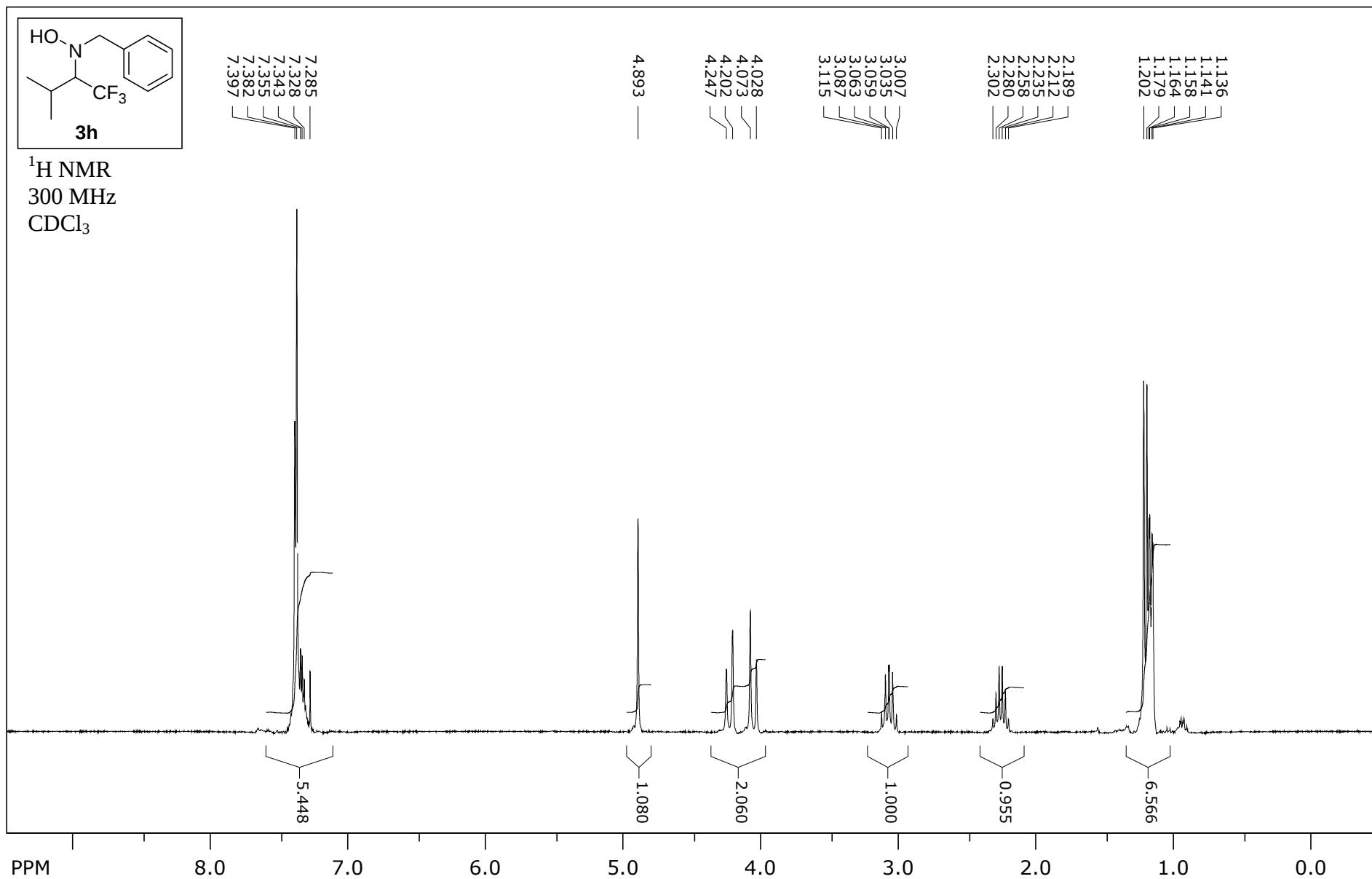


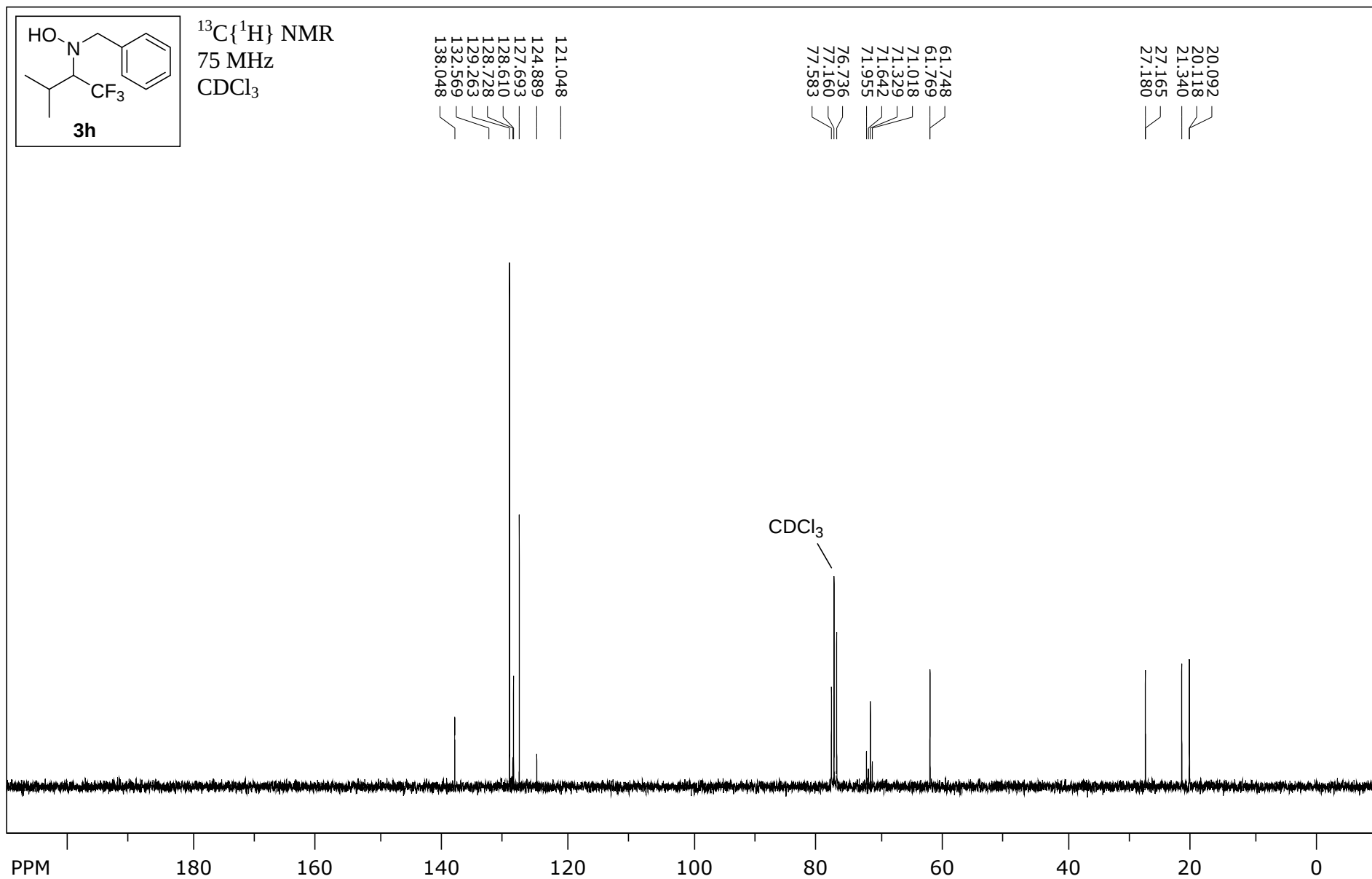


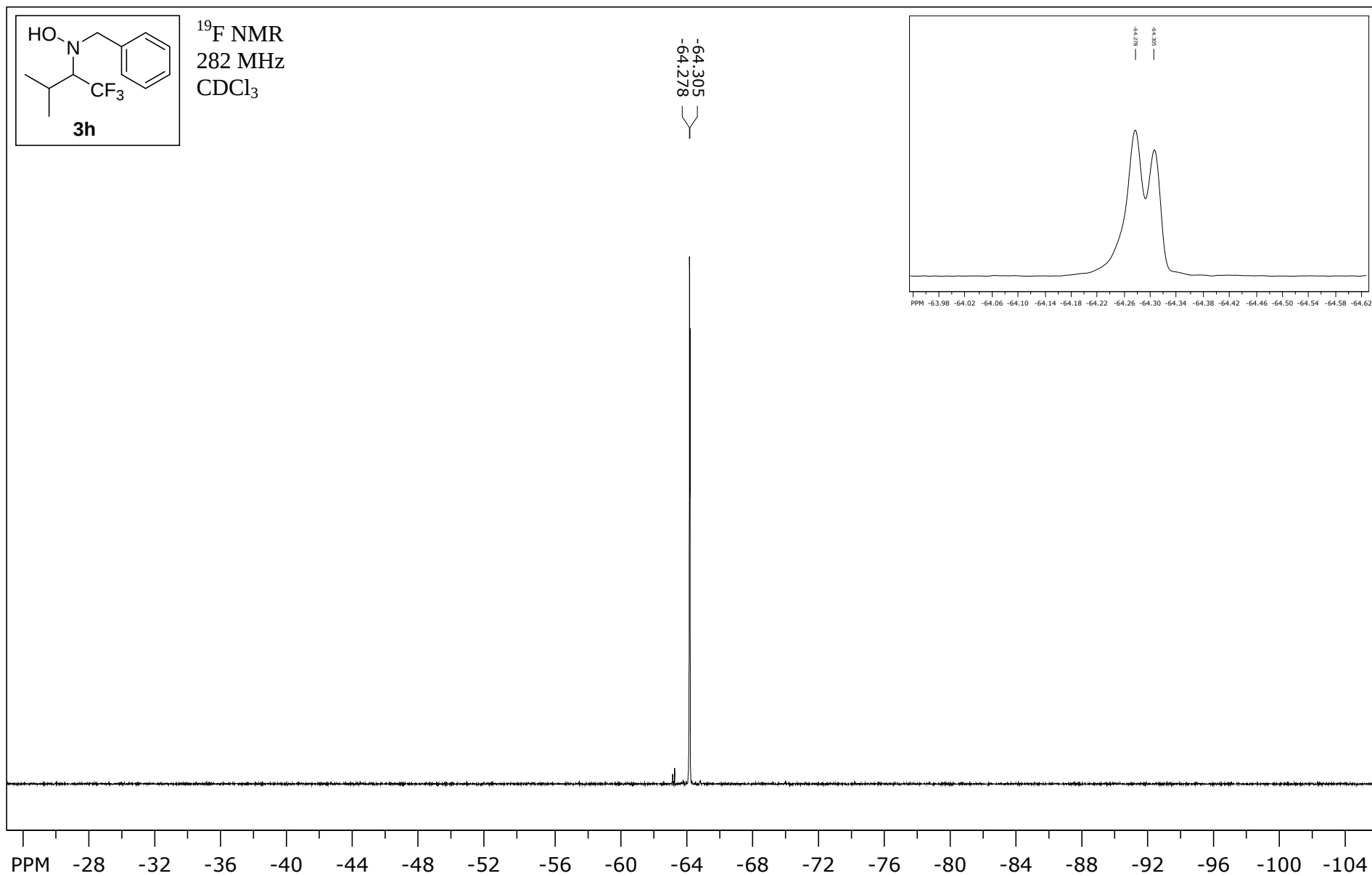












127.758
128.585
129.319
137.635

62.701	
62.729	
62.756	
68.241	
68.489	
68.570	
68.818	
76.738	
77.161	
77.585	

20.785	—
20.827	—
20.868	—
22.837	—
22.881	—
26.475	—

 CDCl_3

PPM

180

160

140

120

100

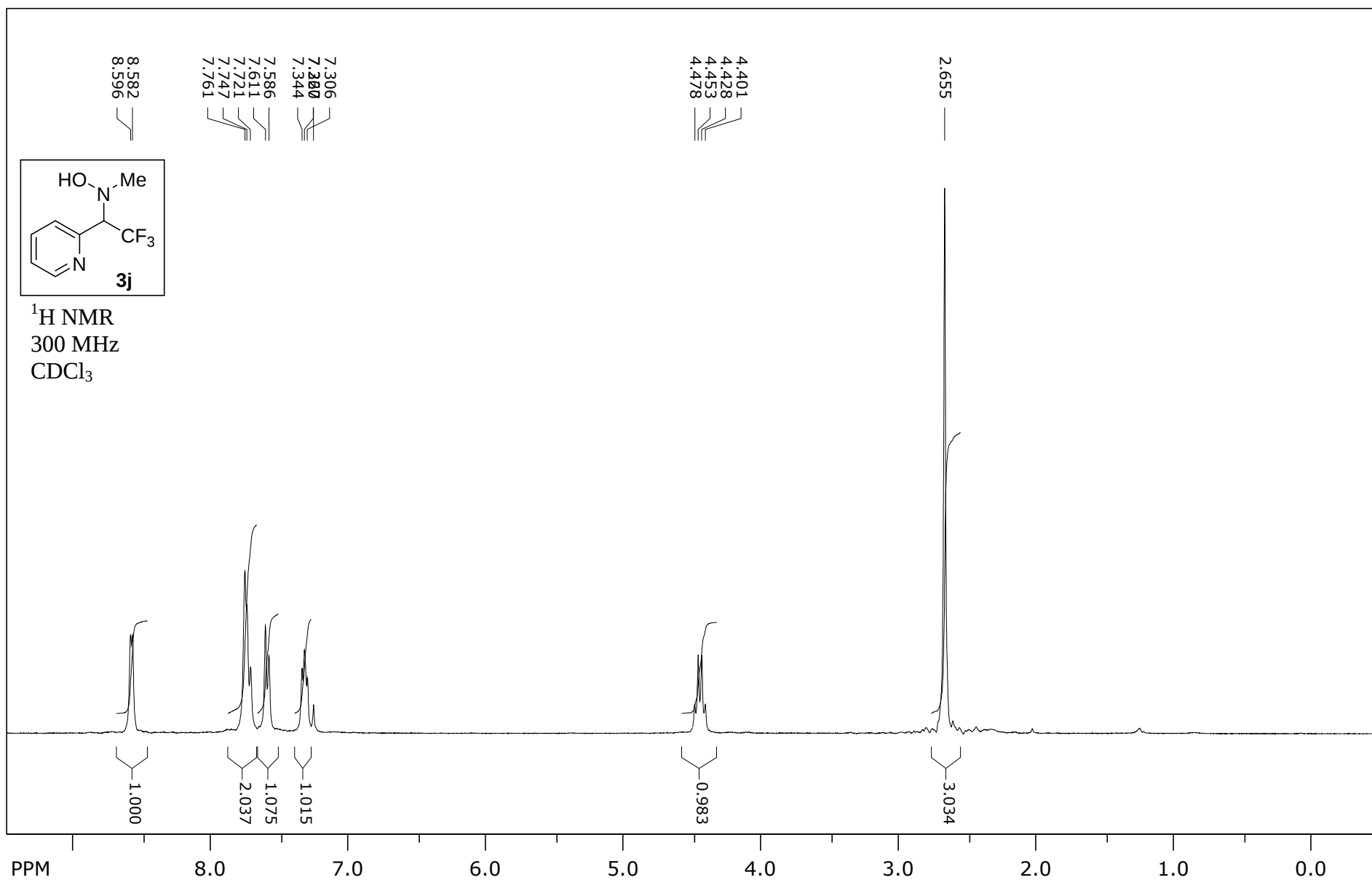
80

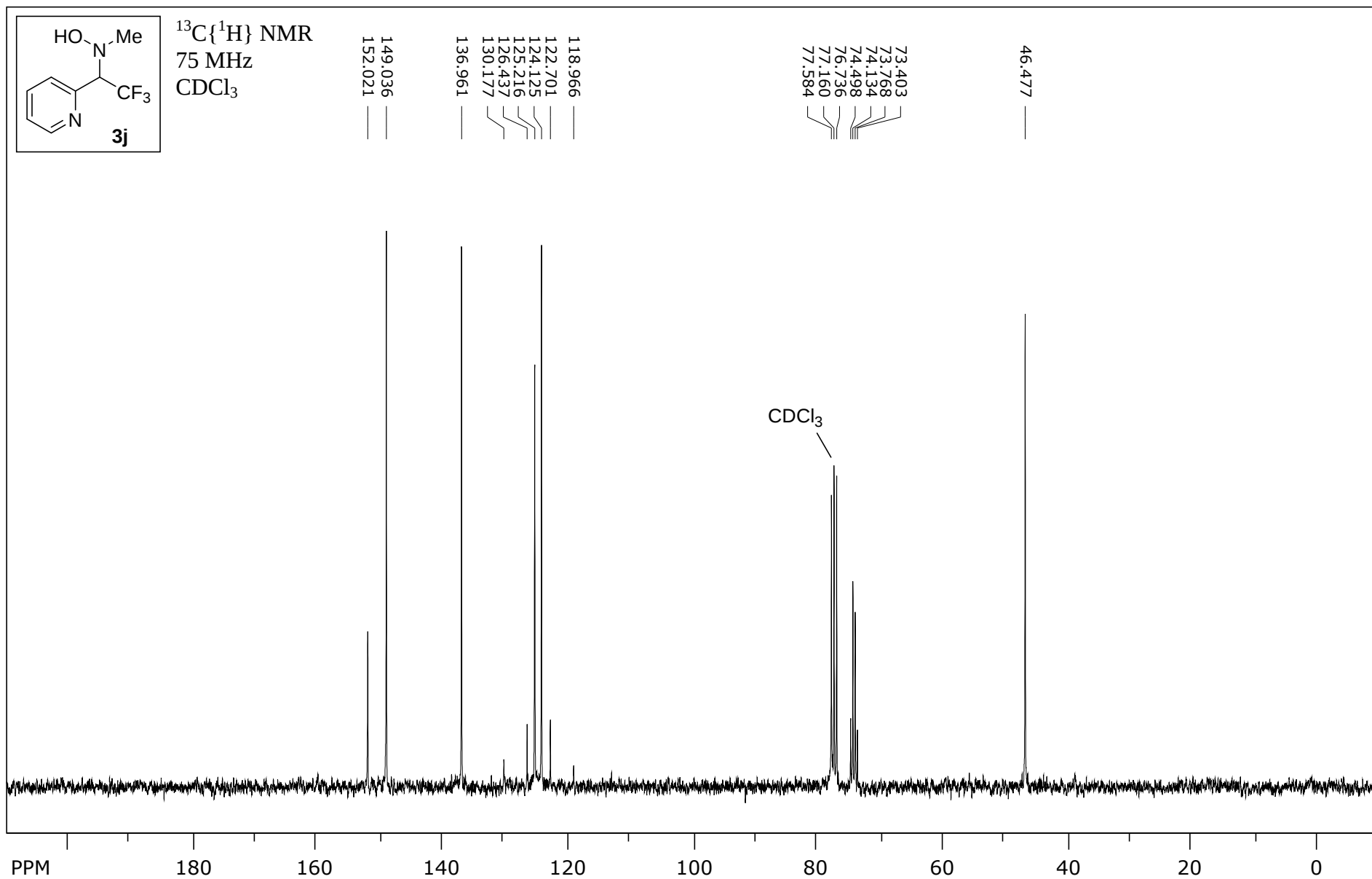
60

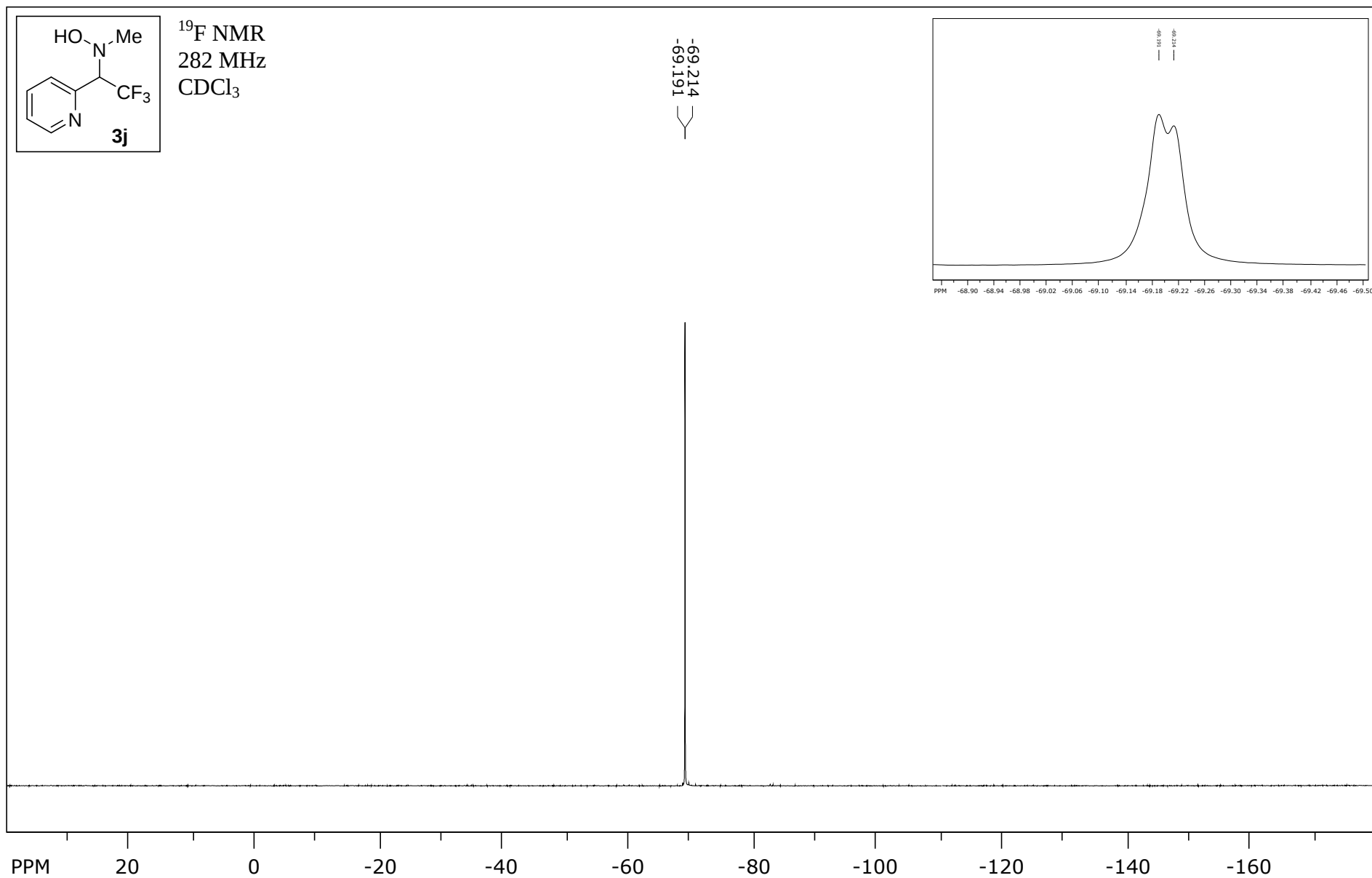
40

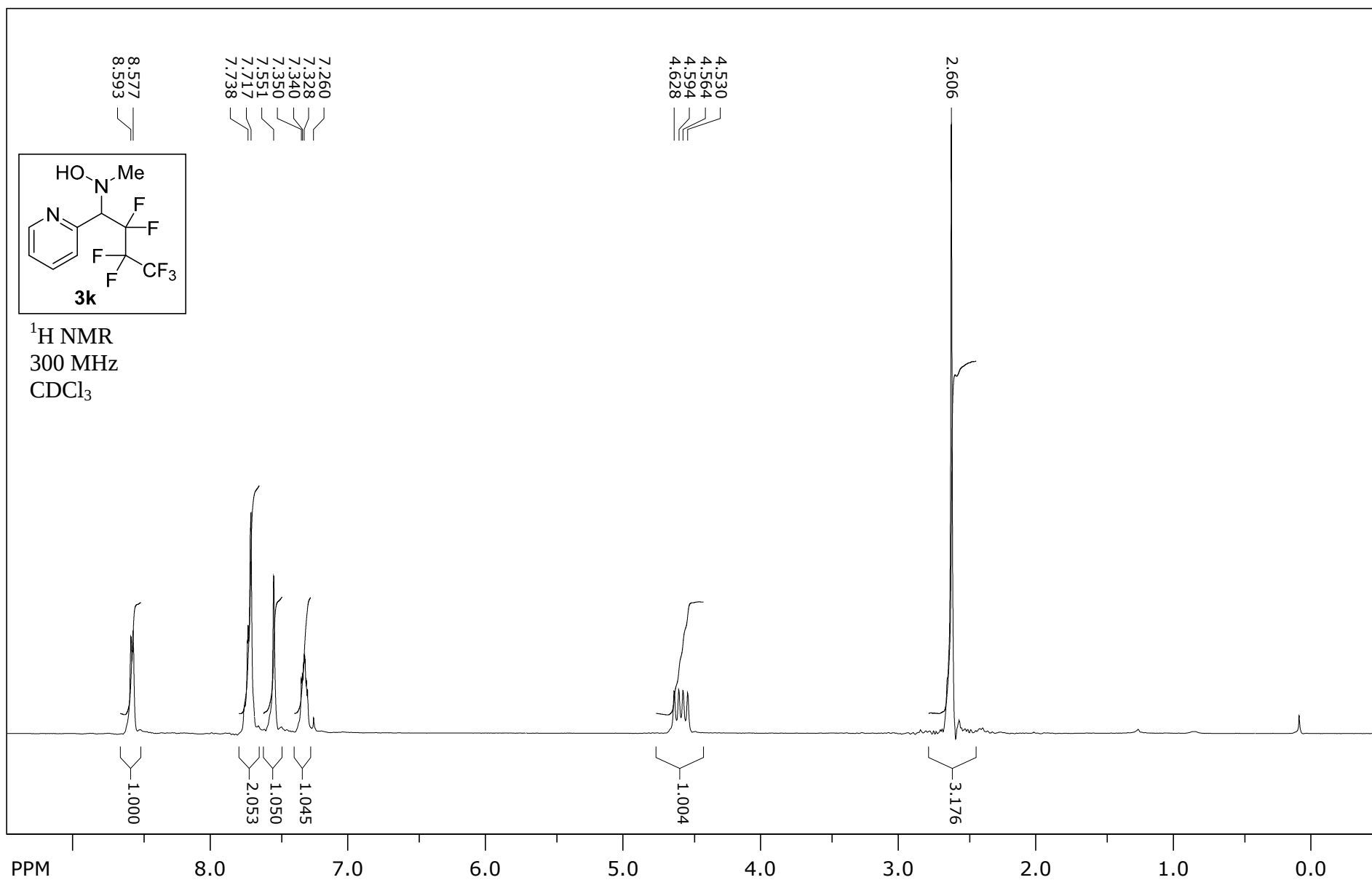
20

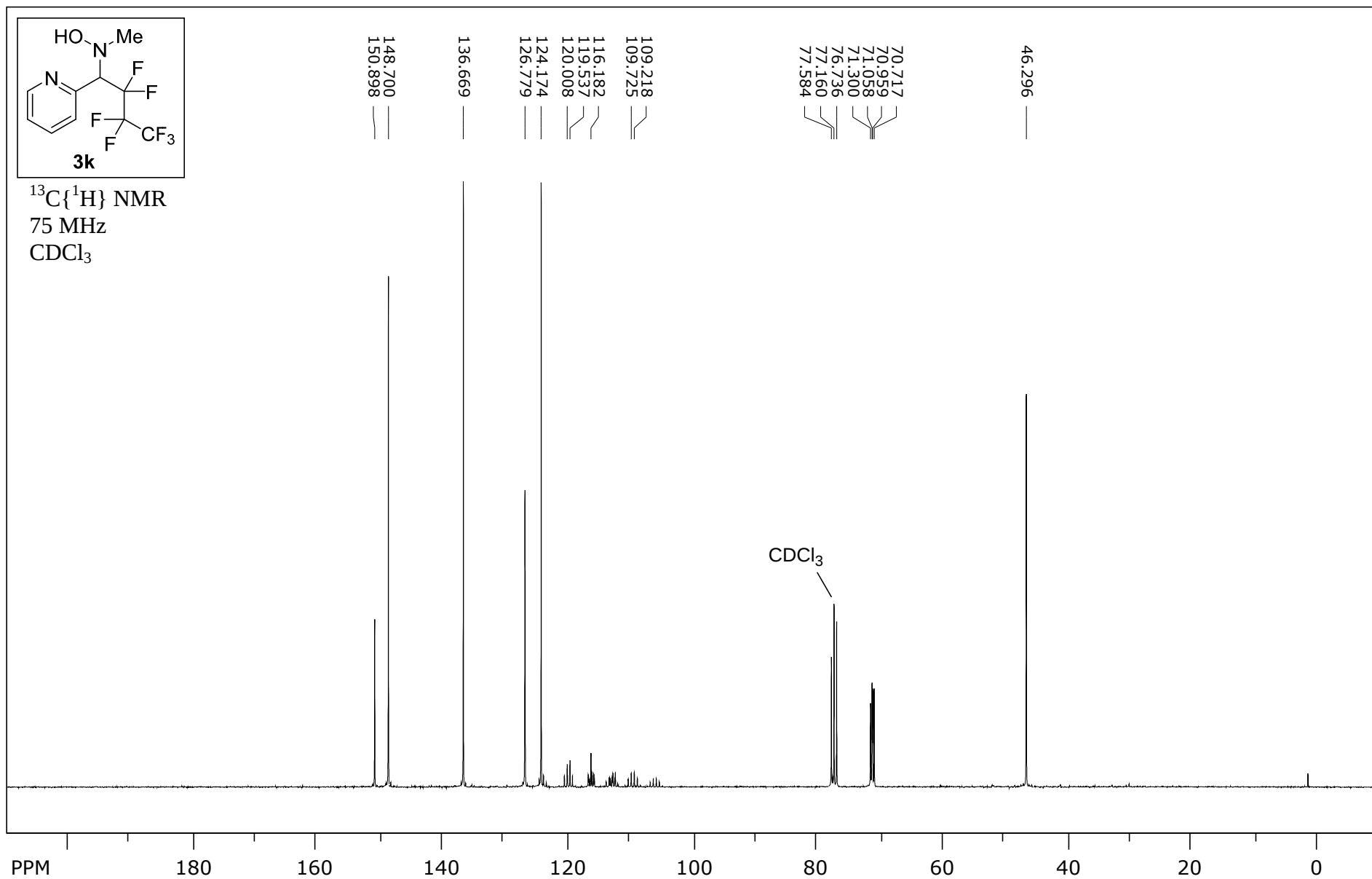
0

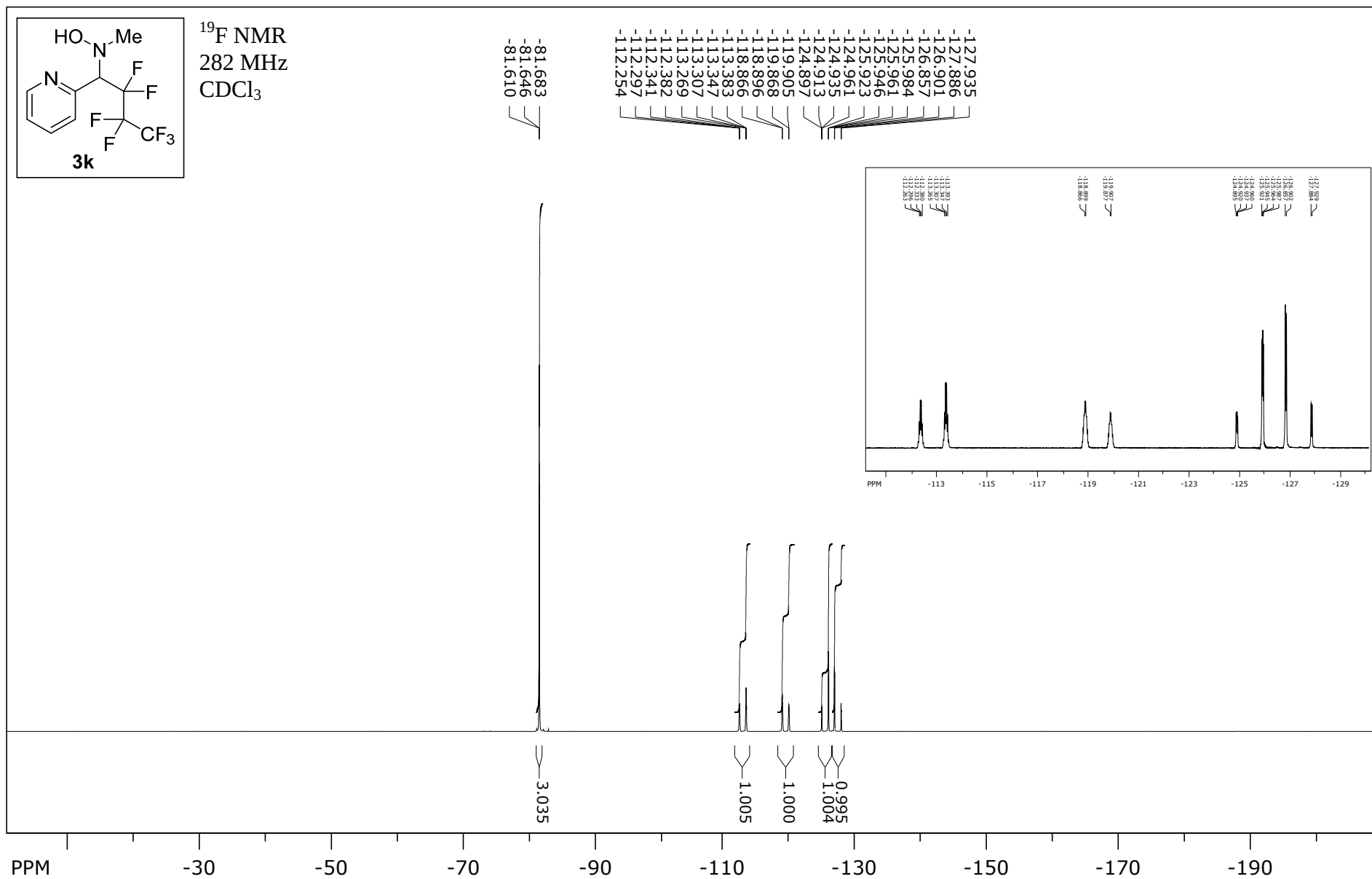


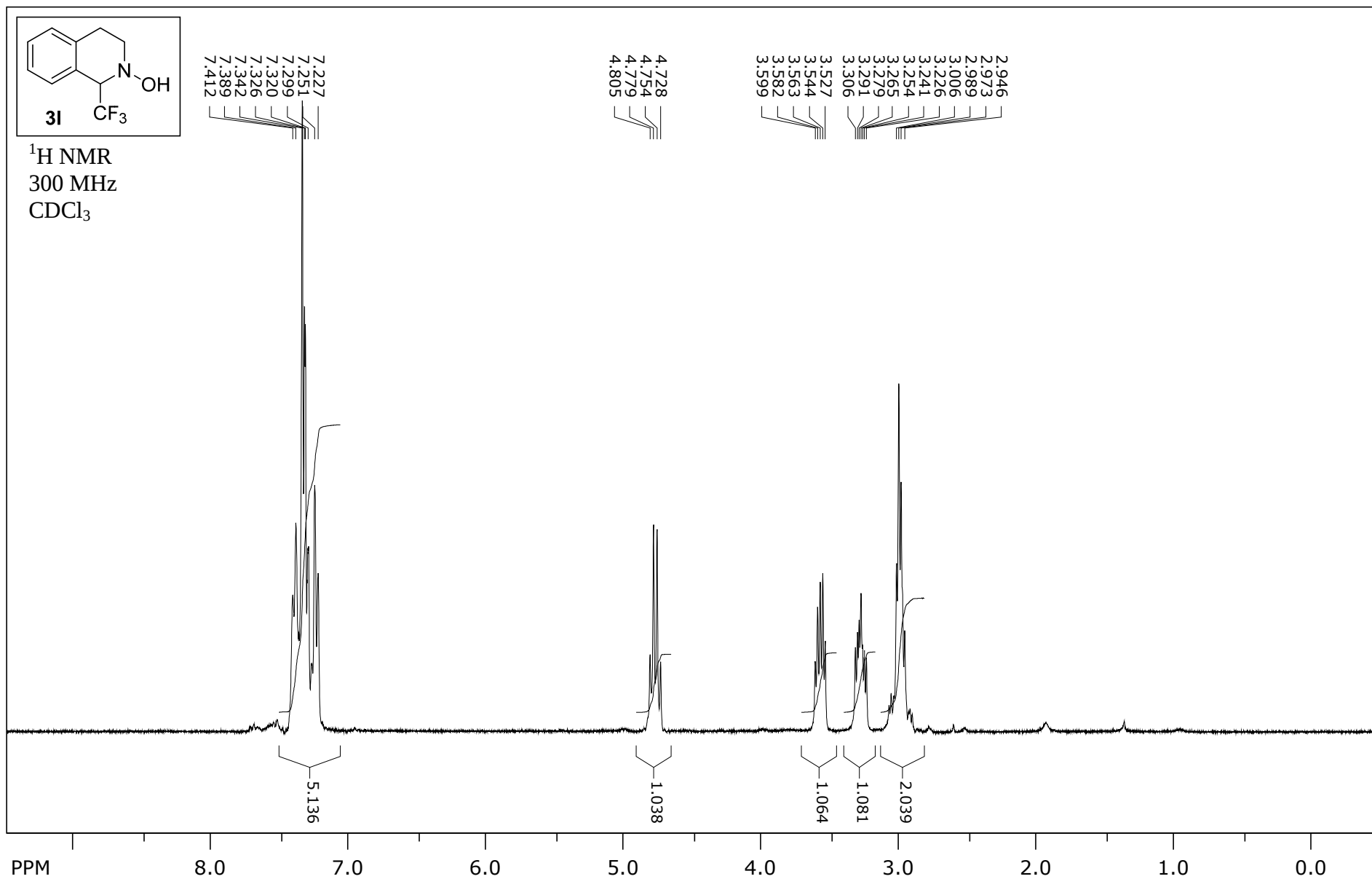


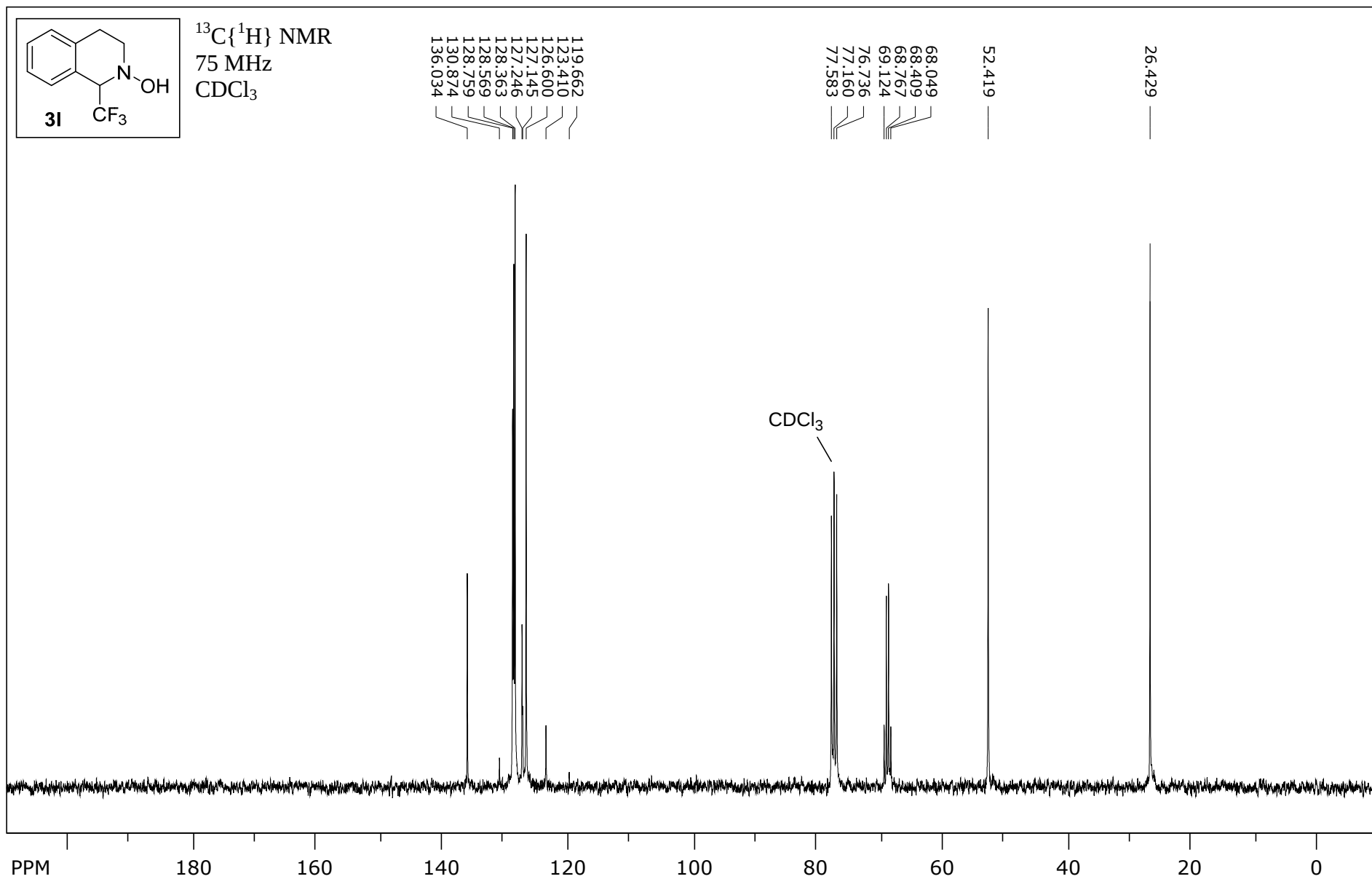


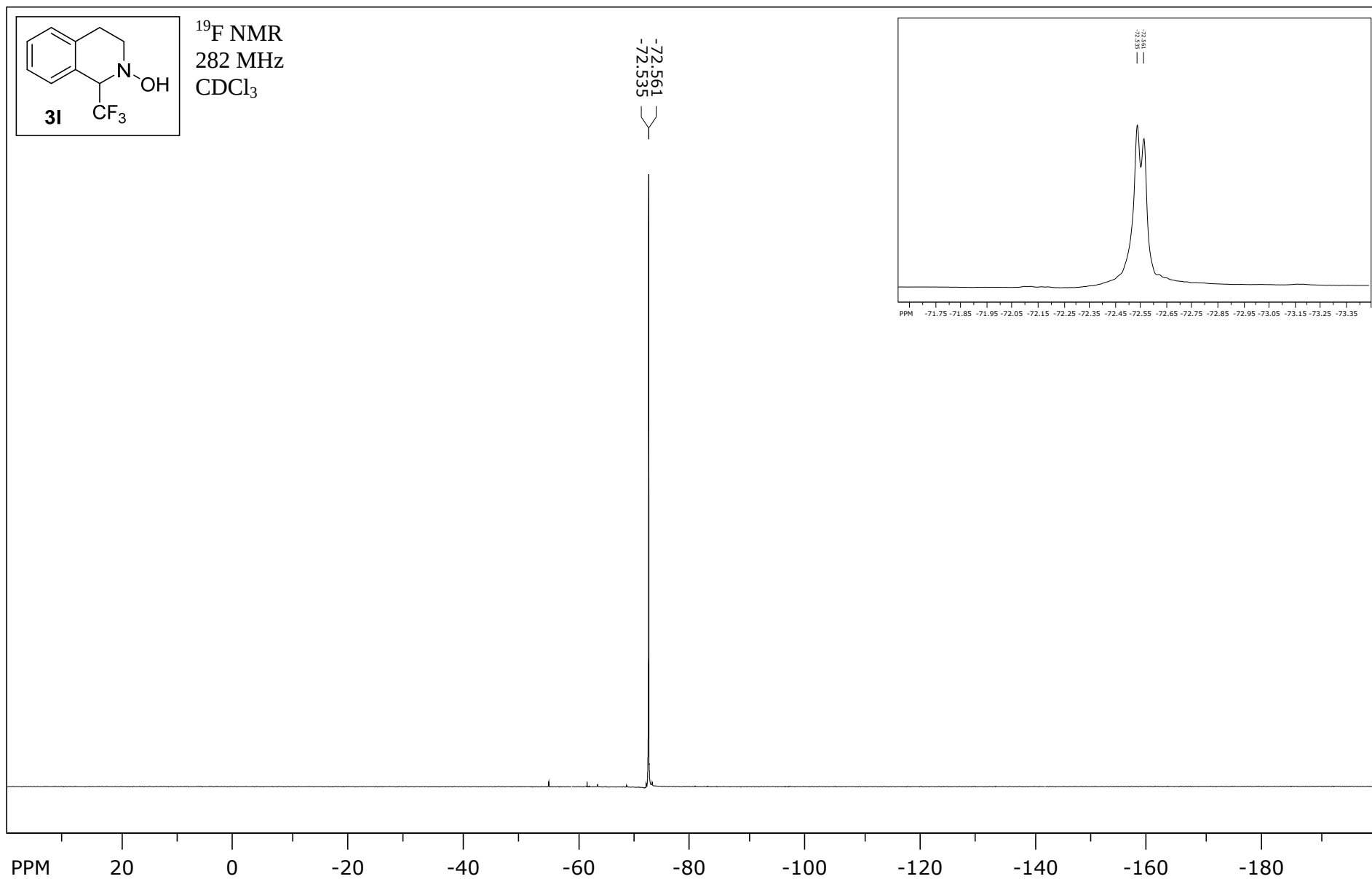


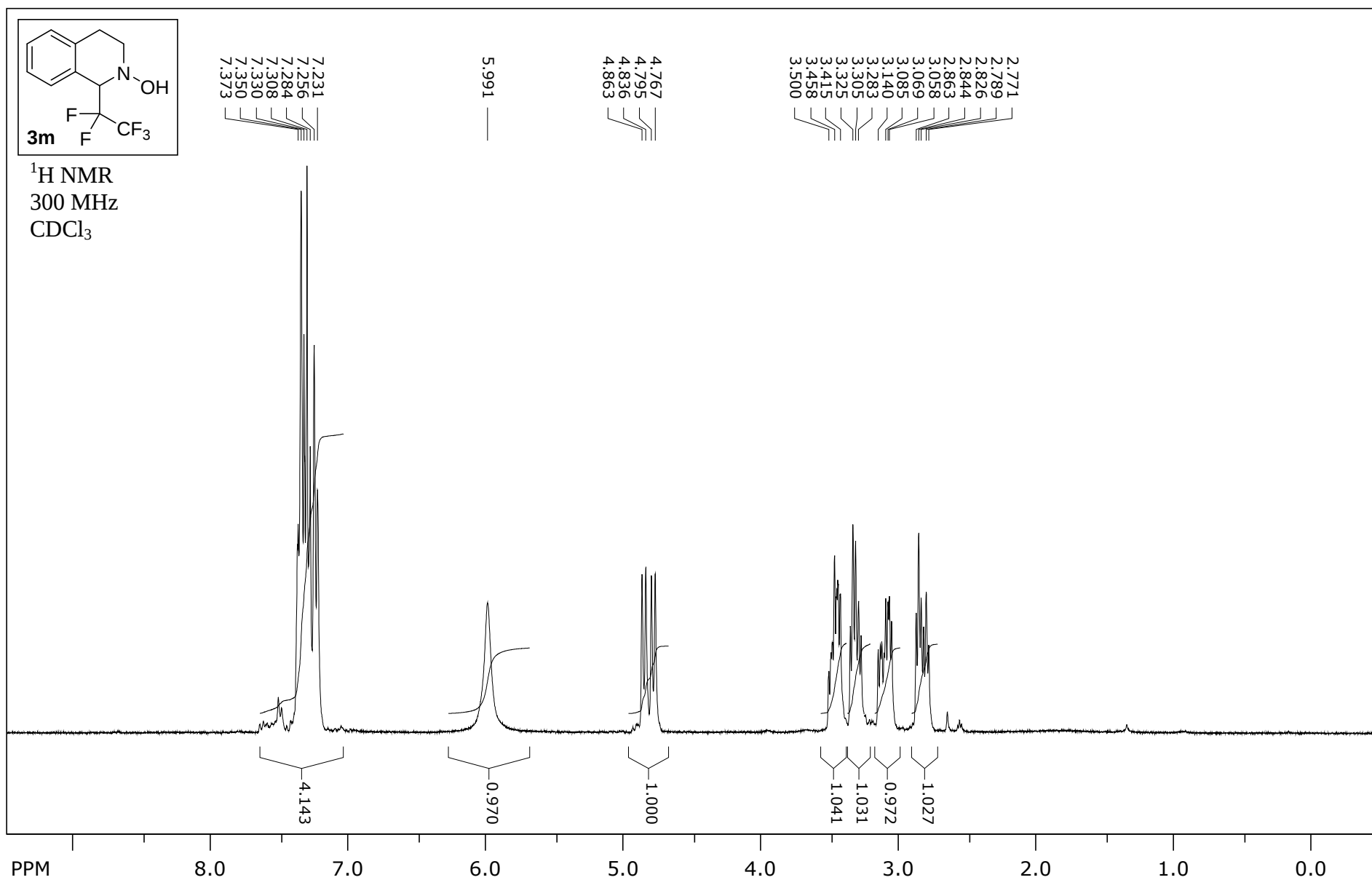


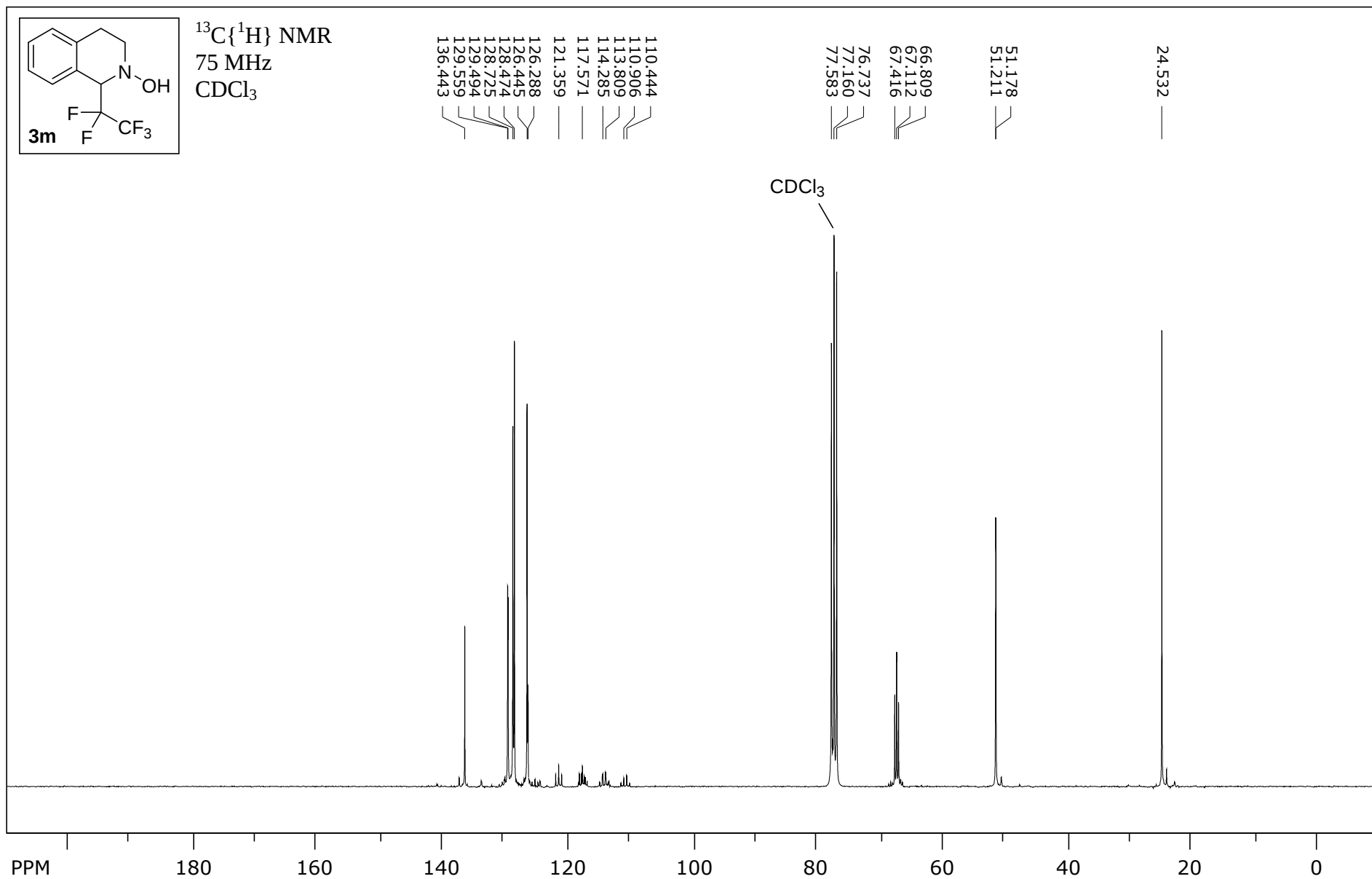


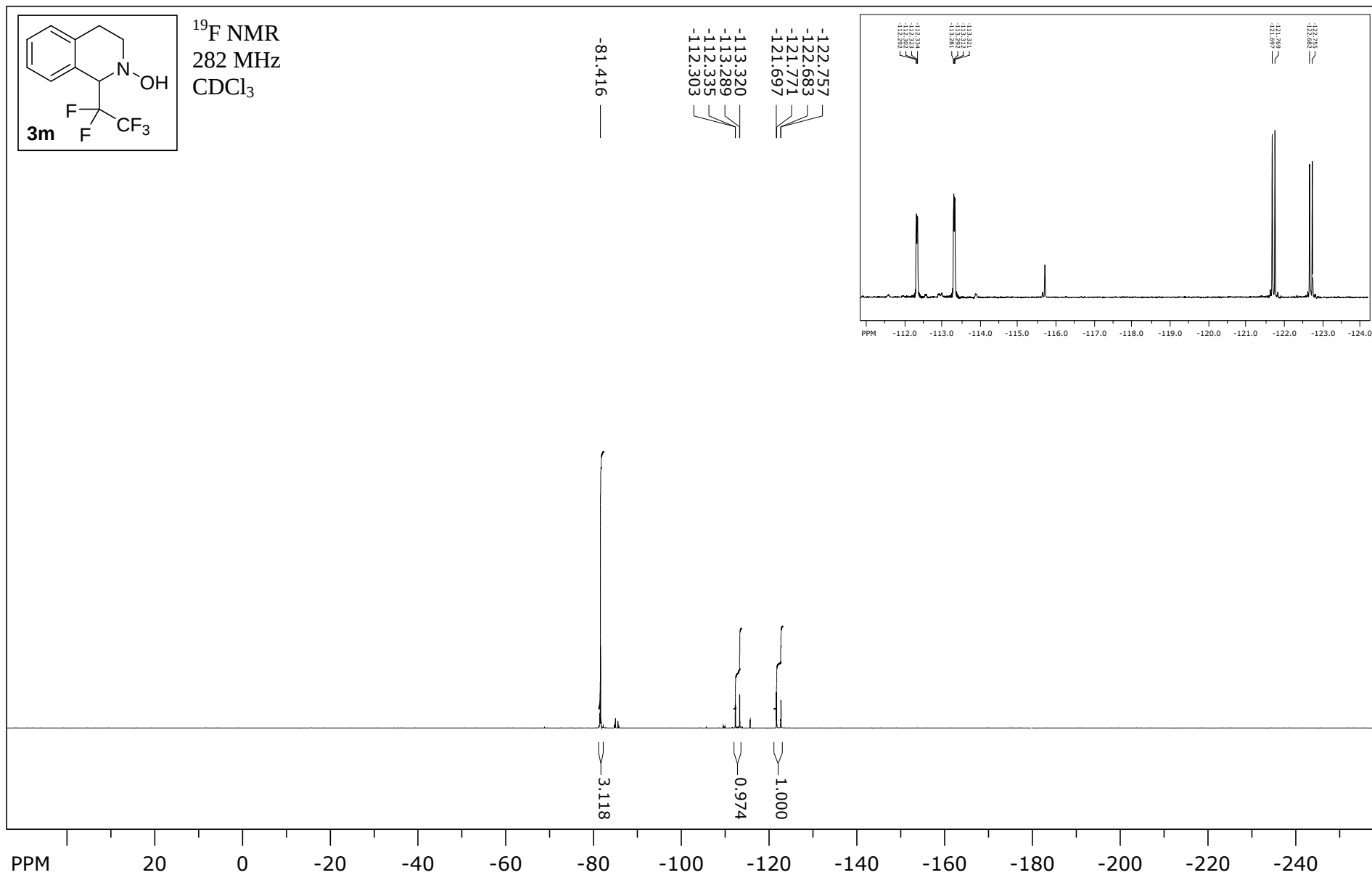


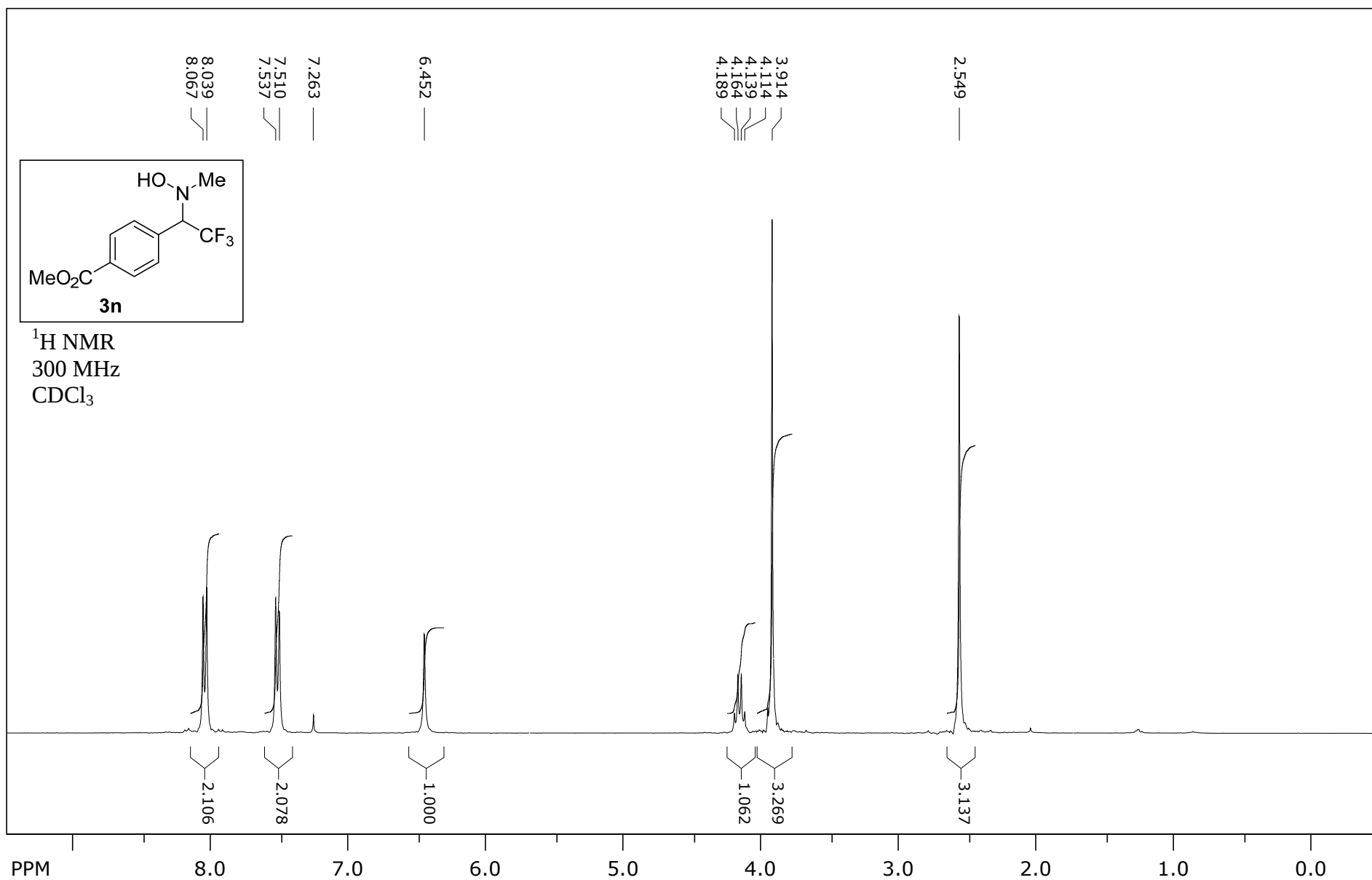


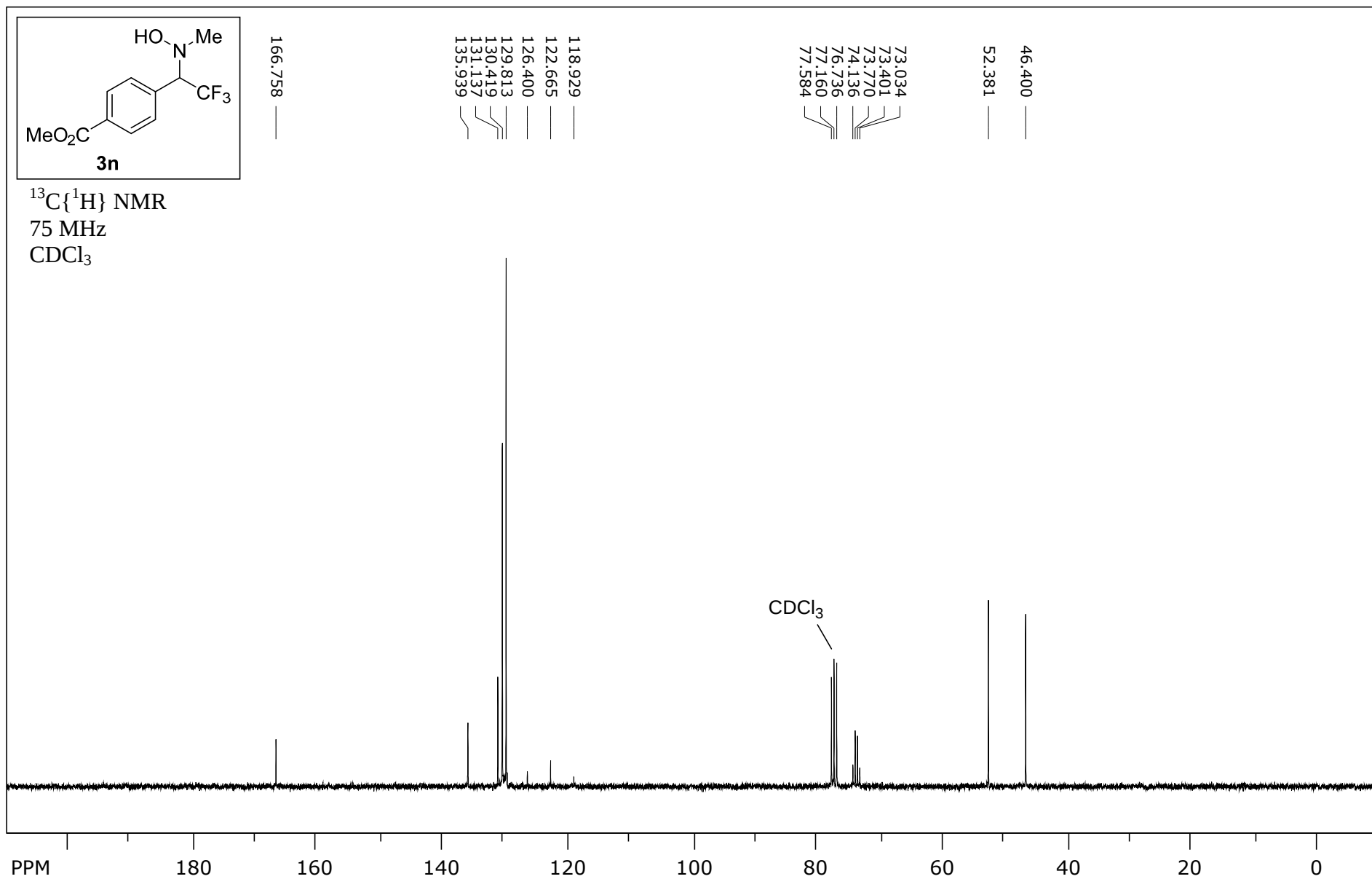


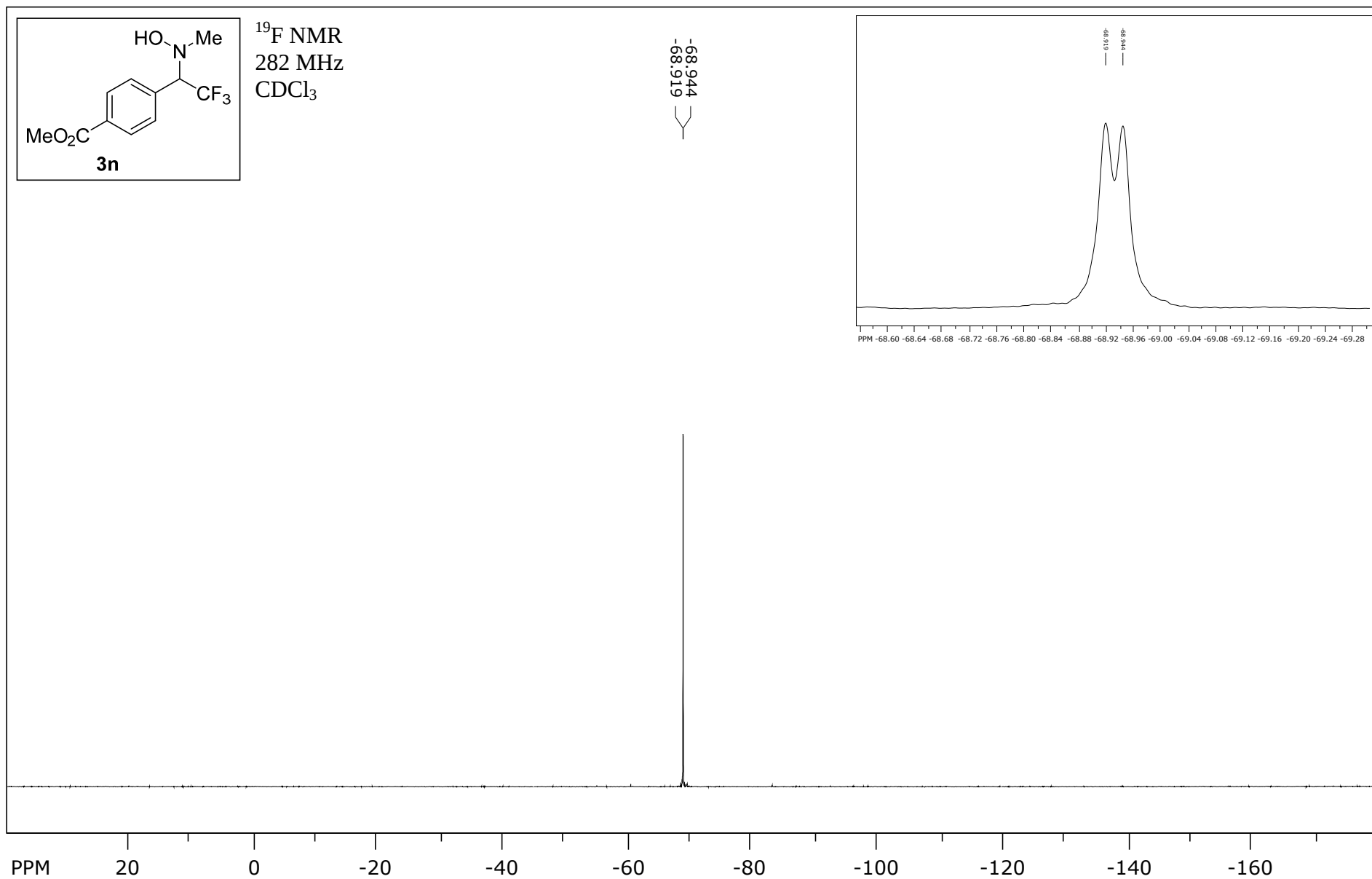


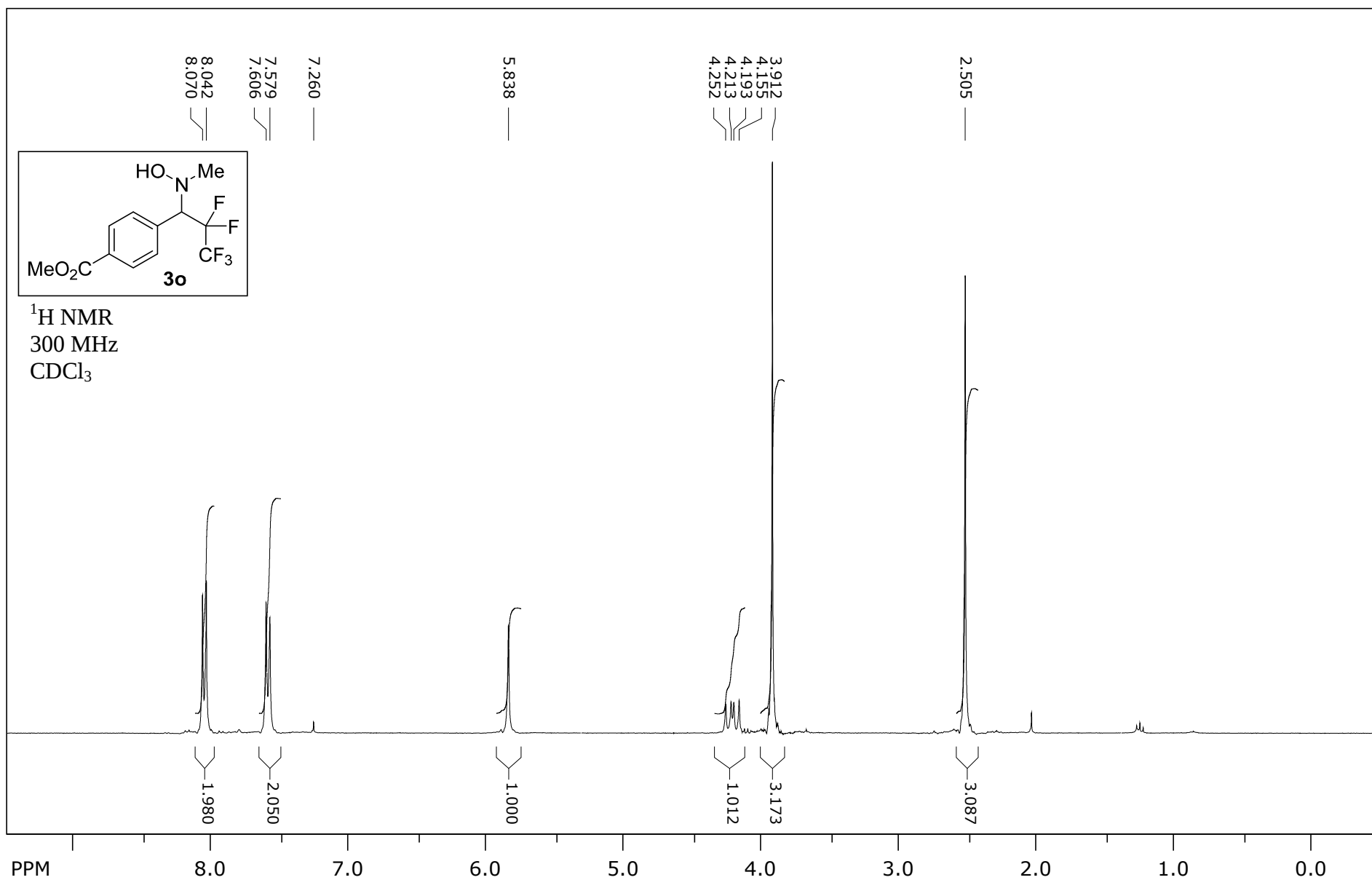


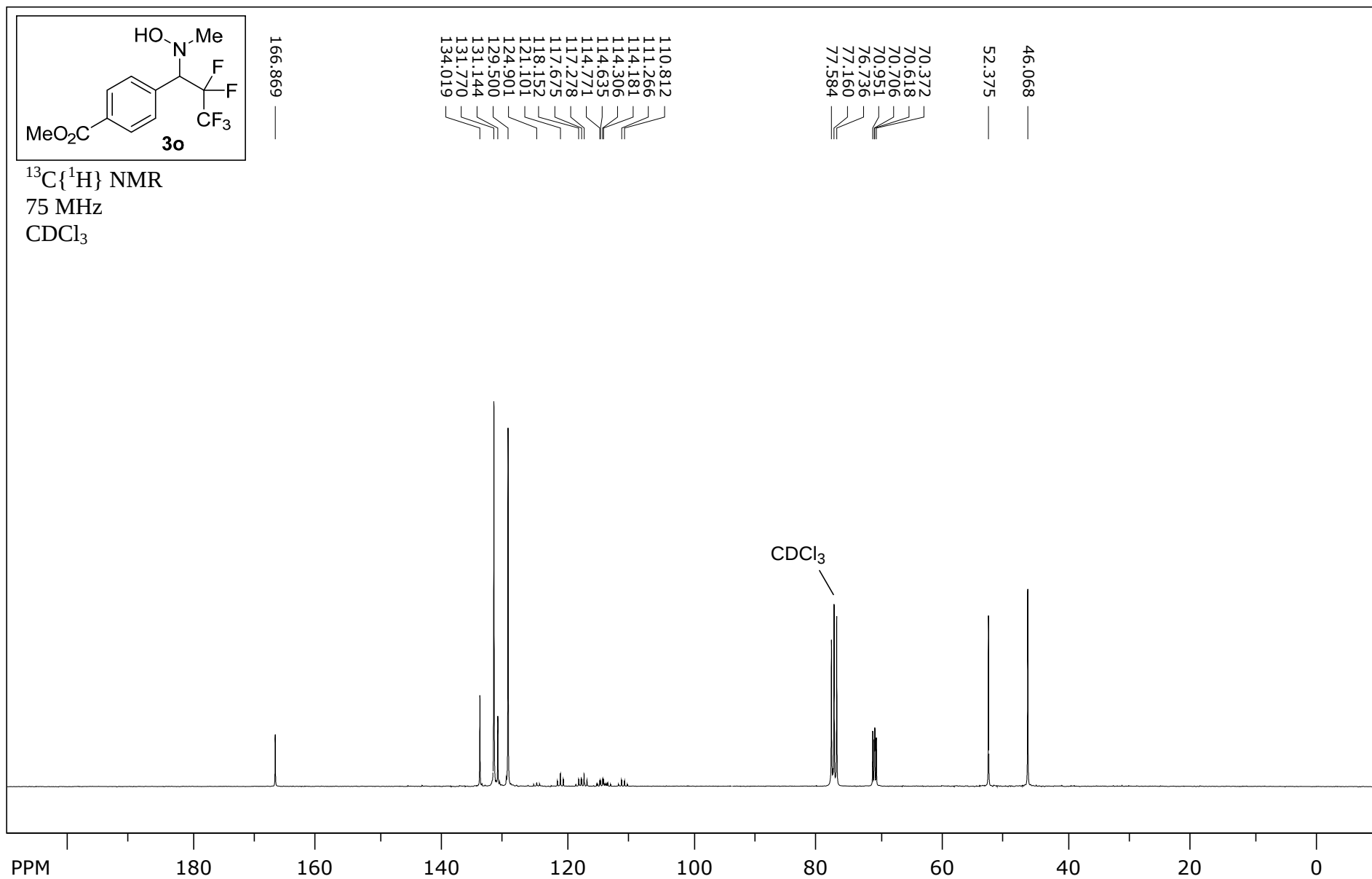


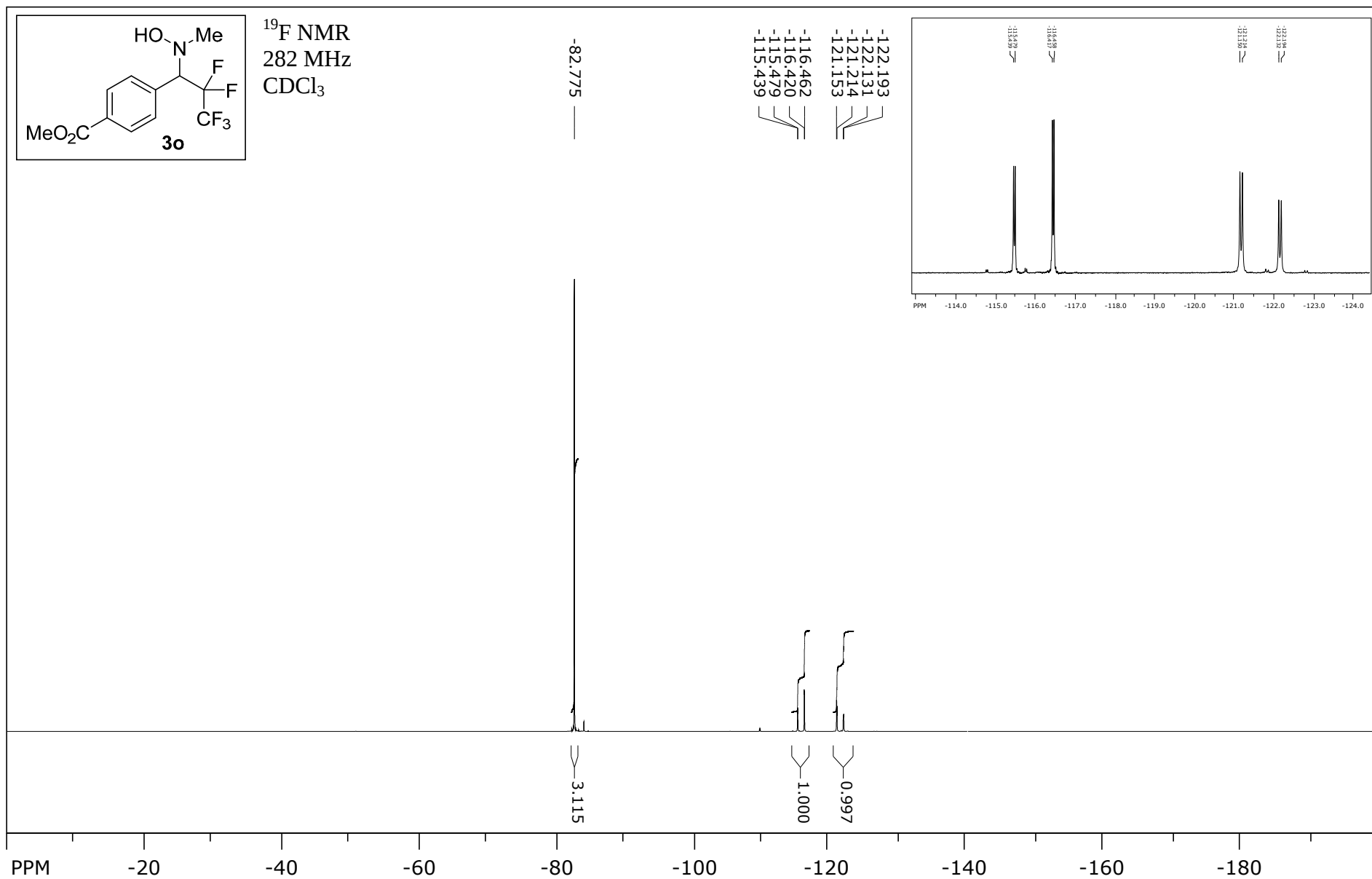


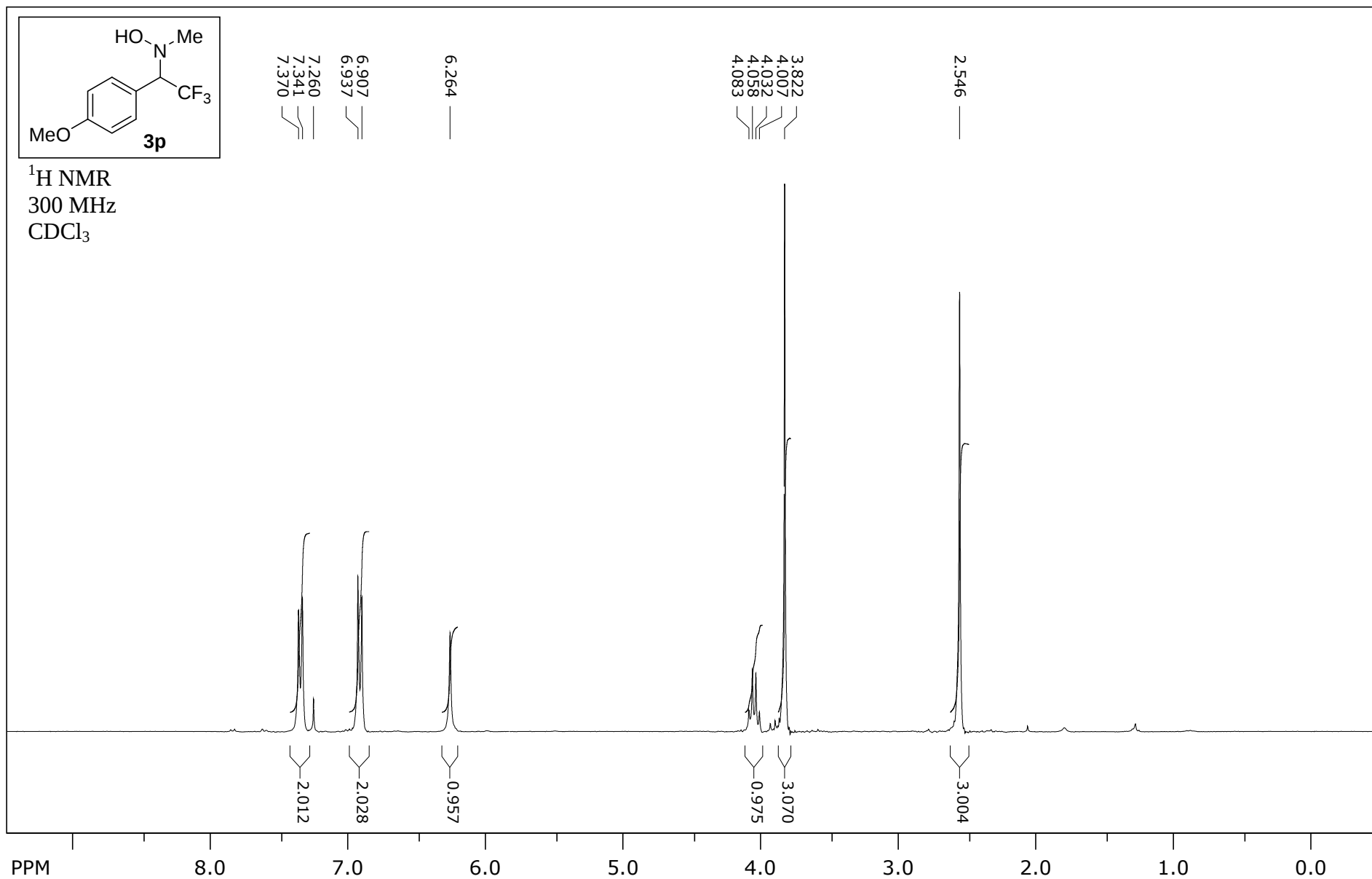


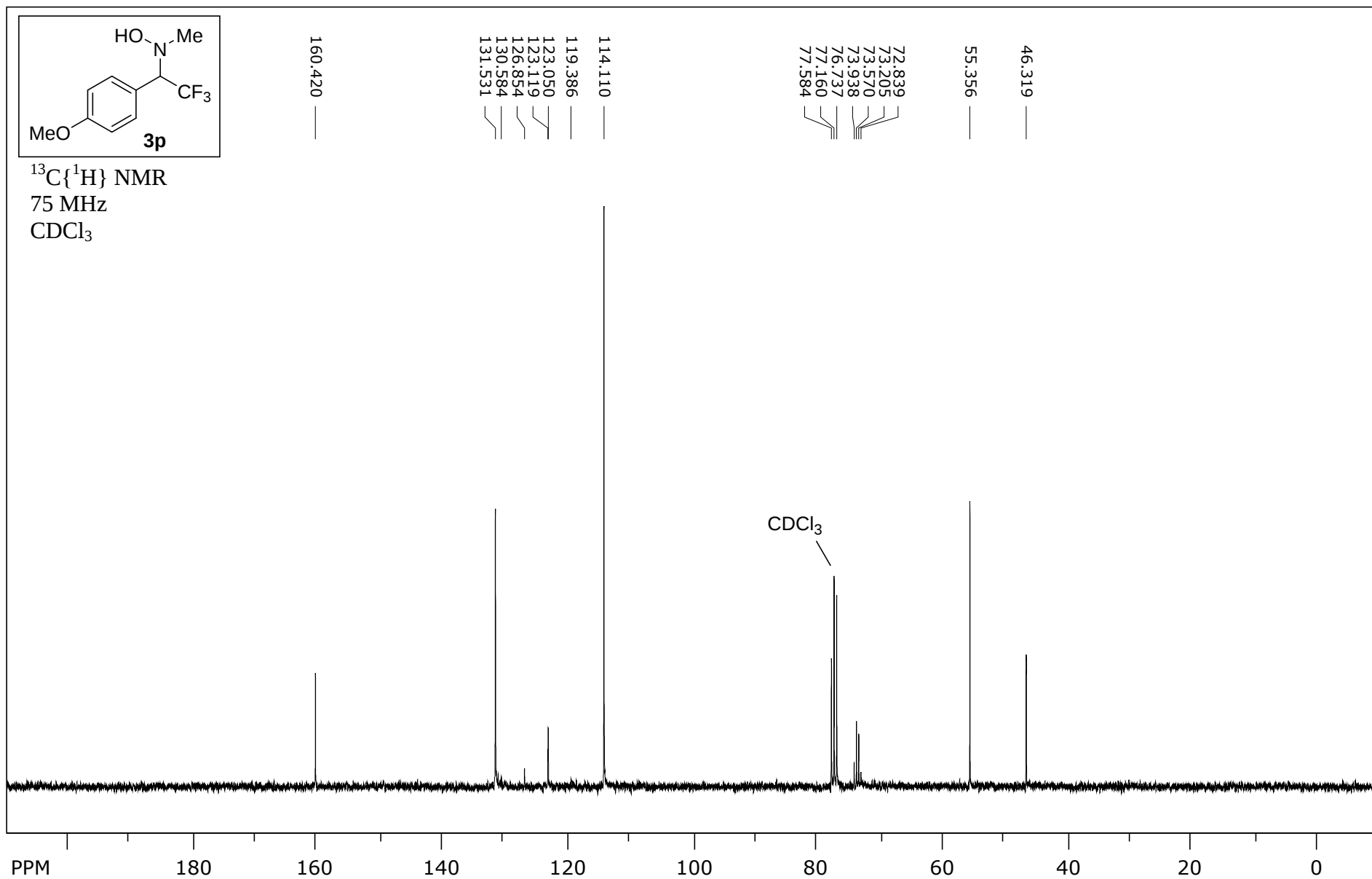


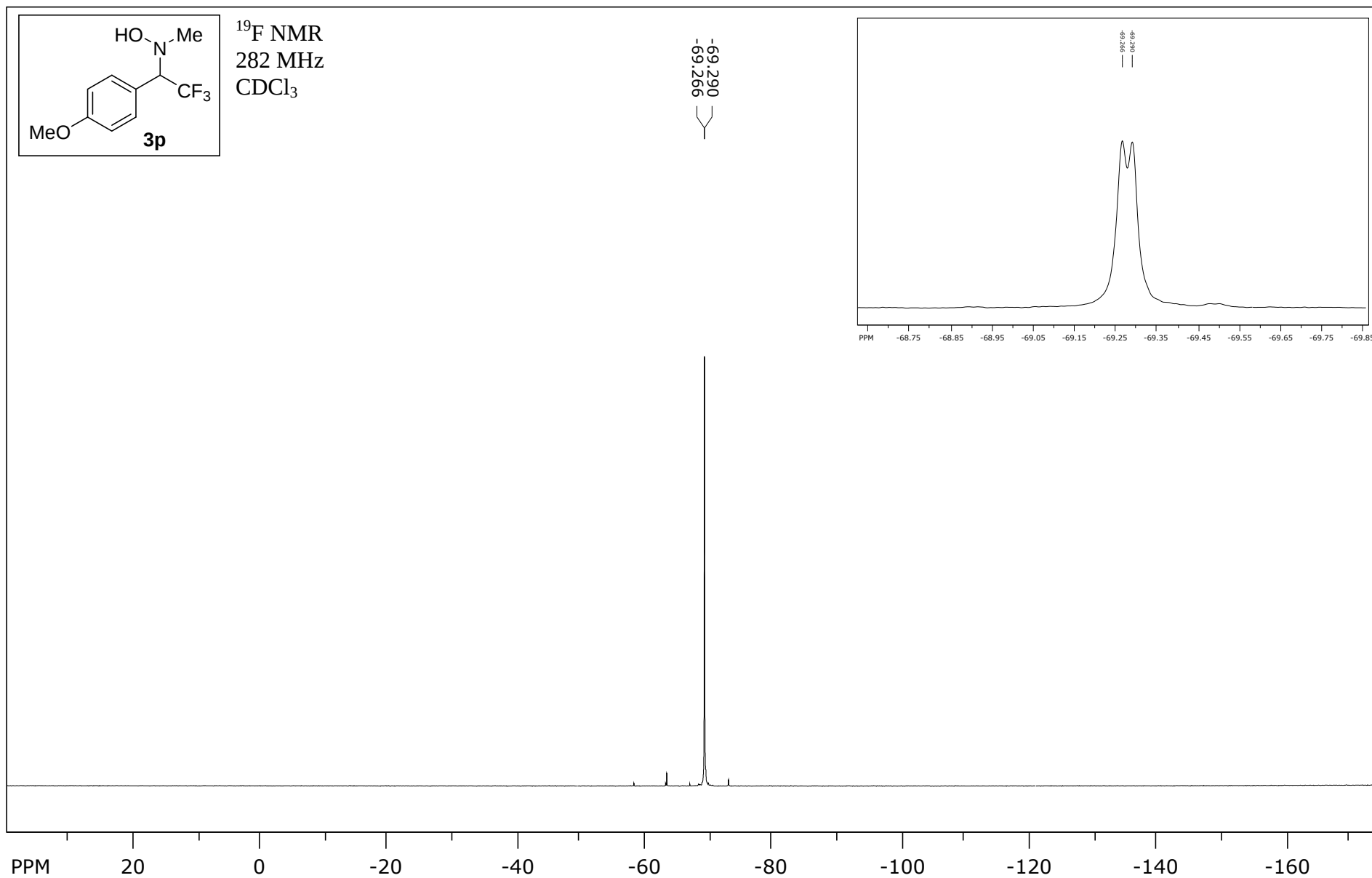


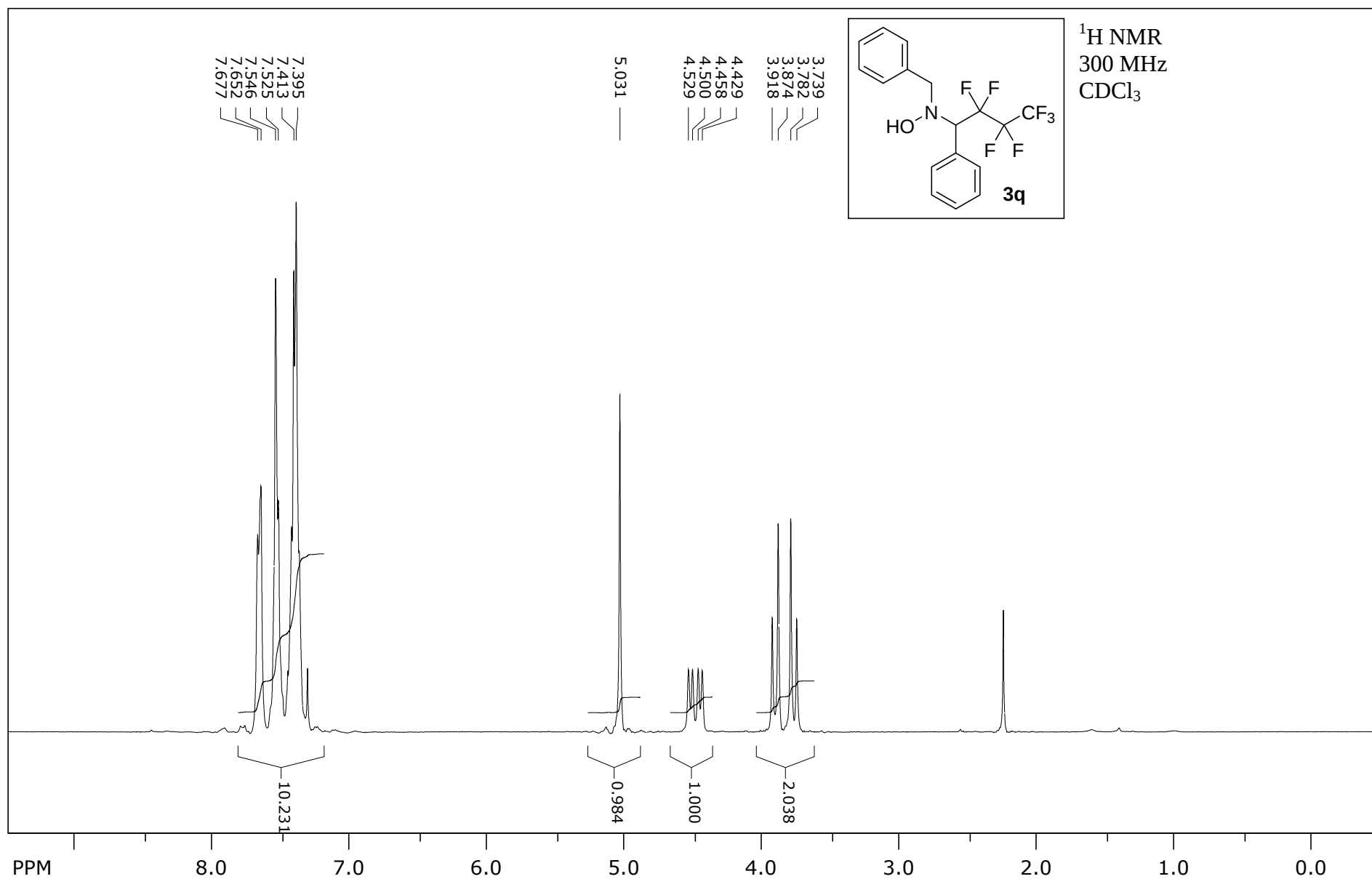


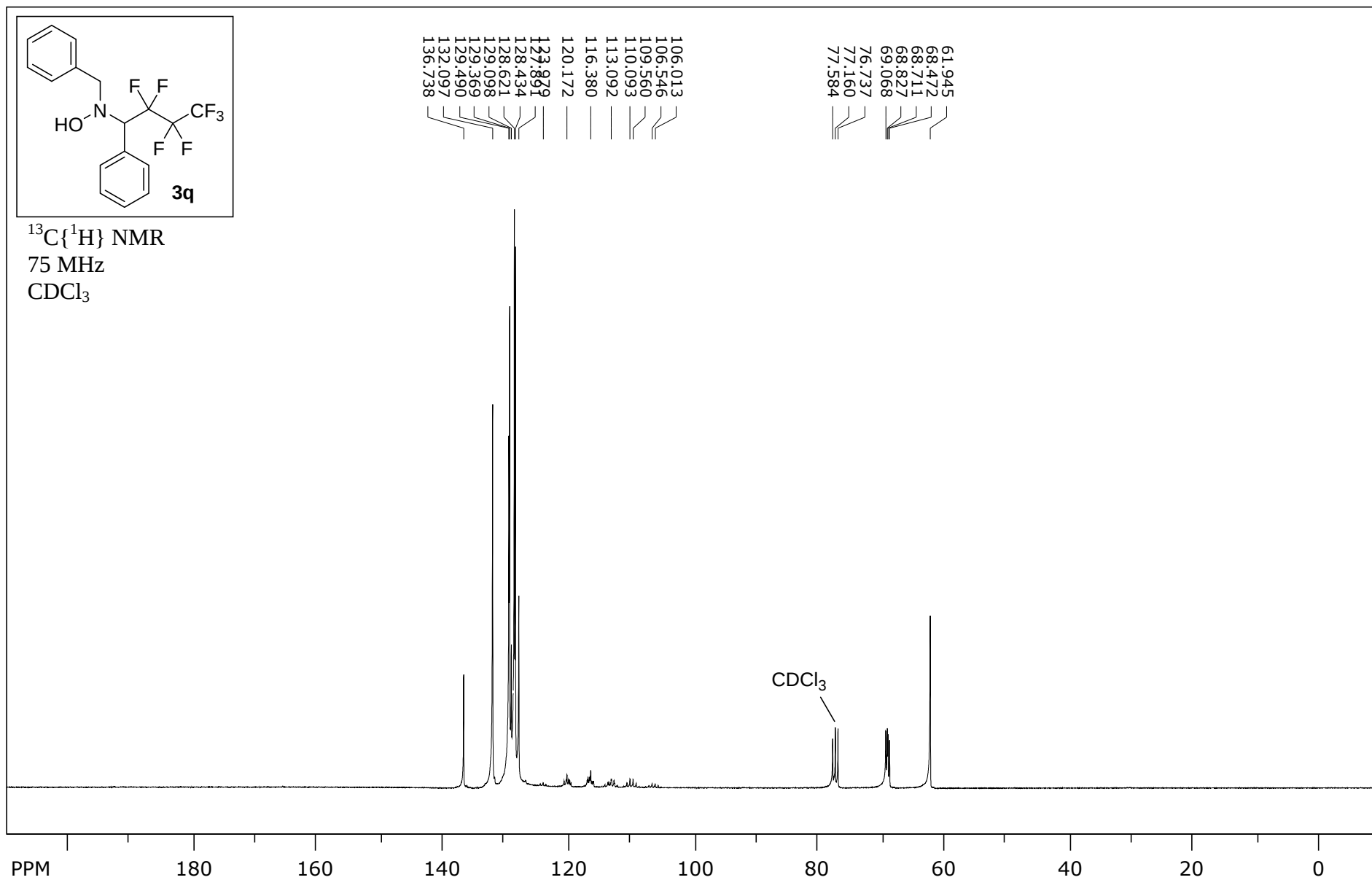


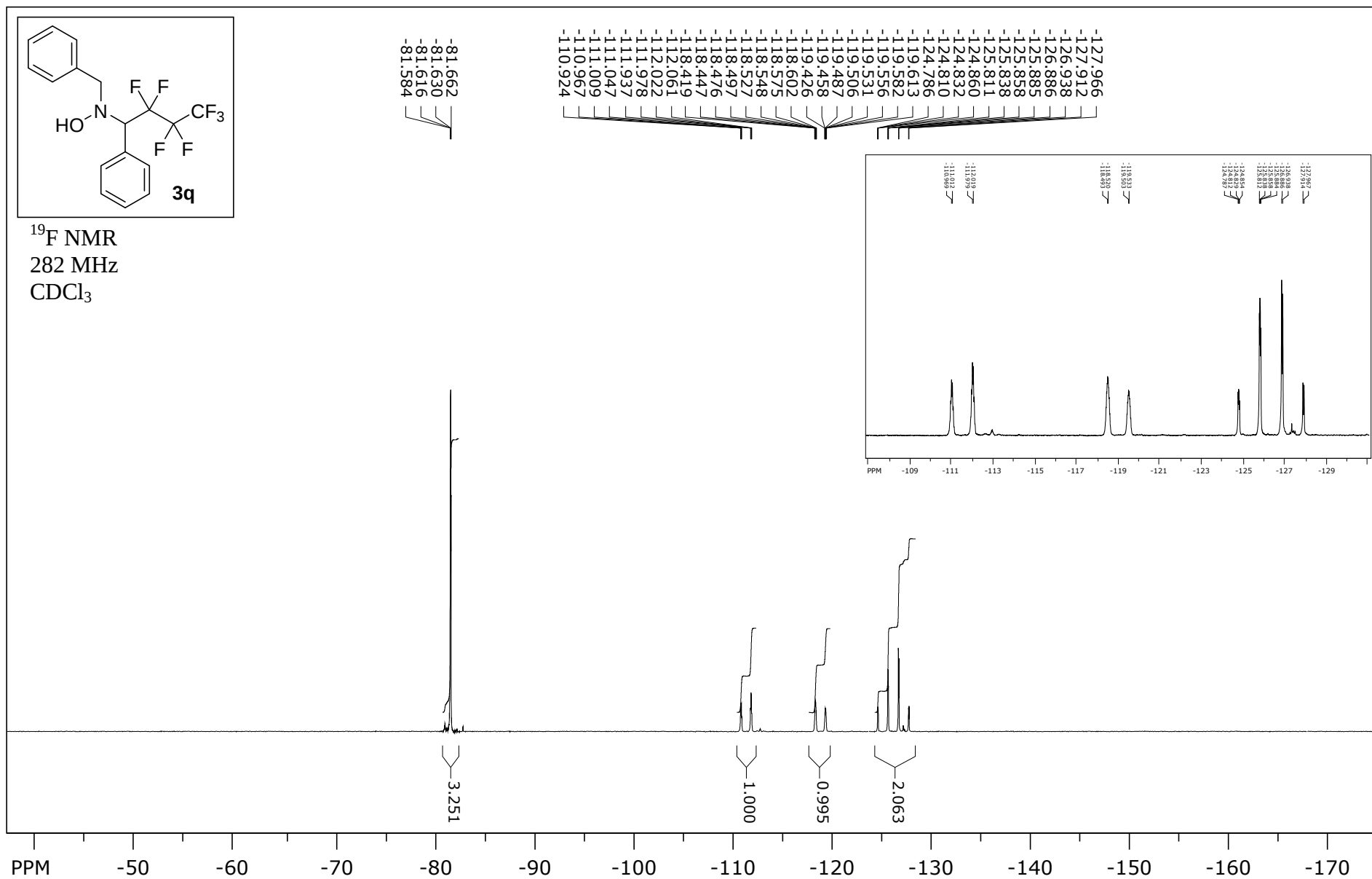


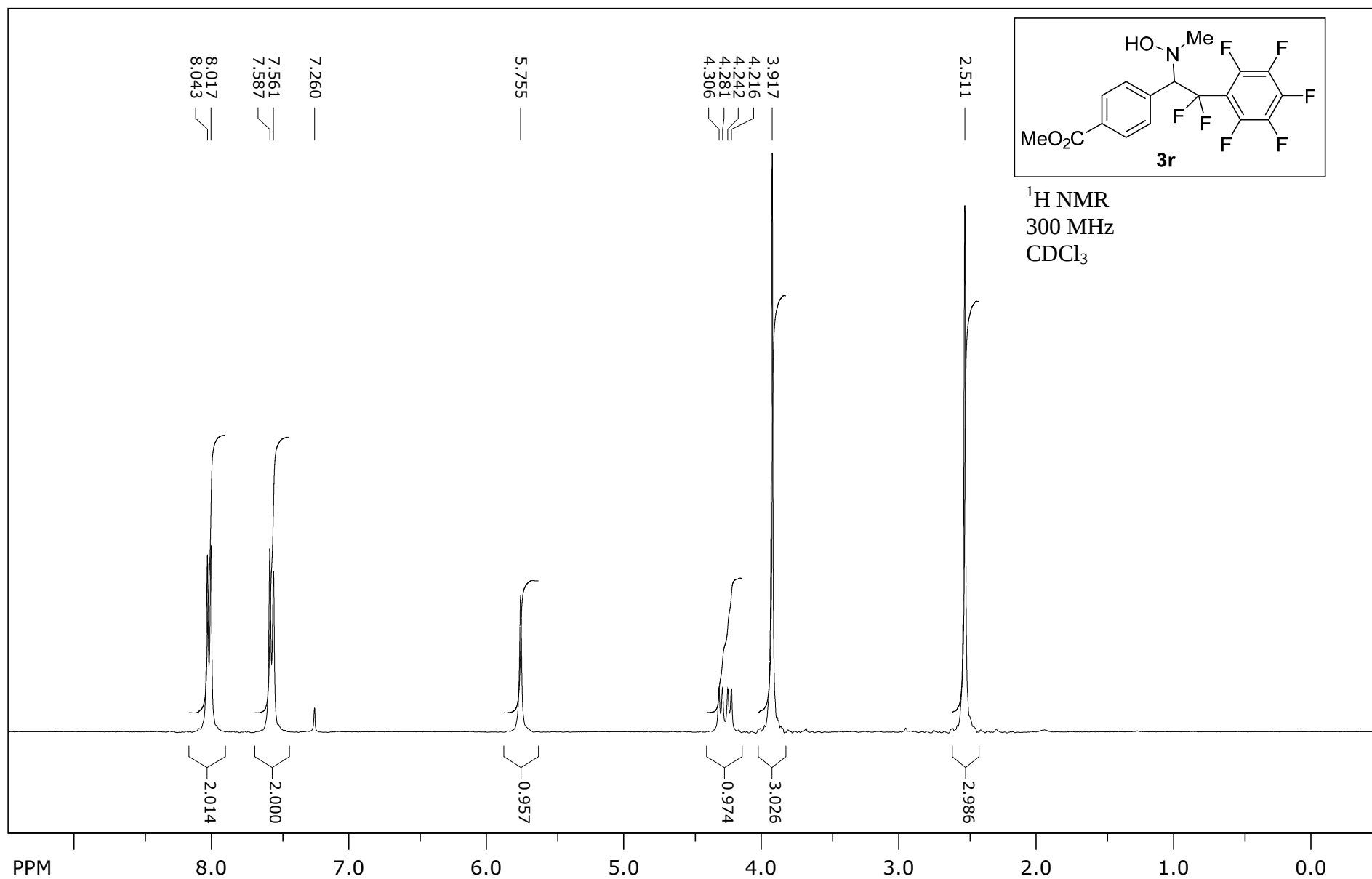


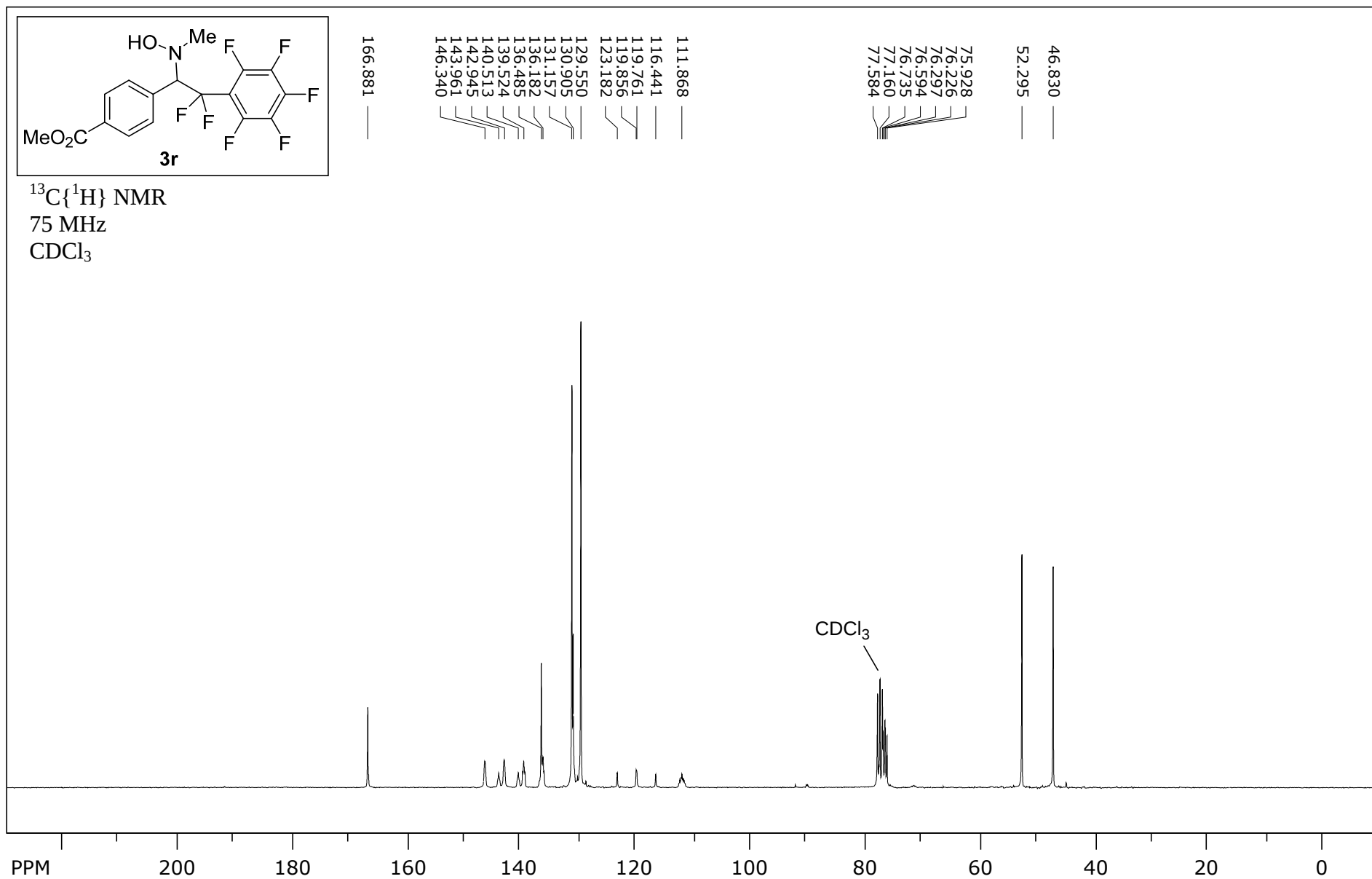


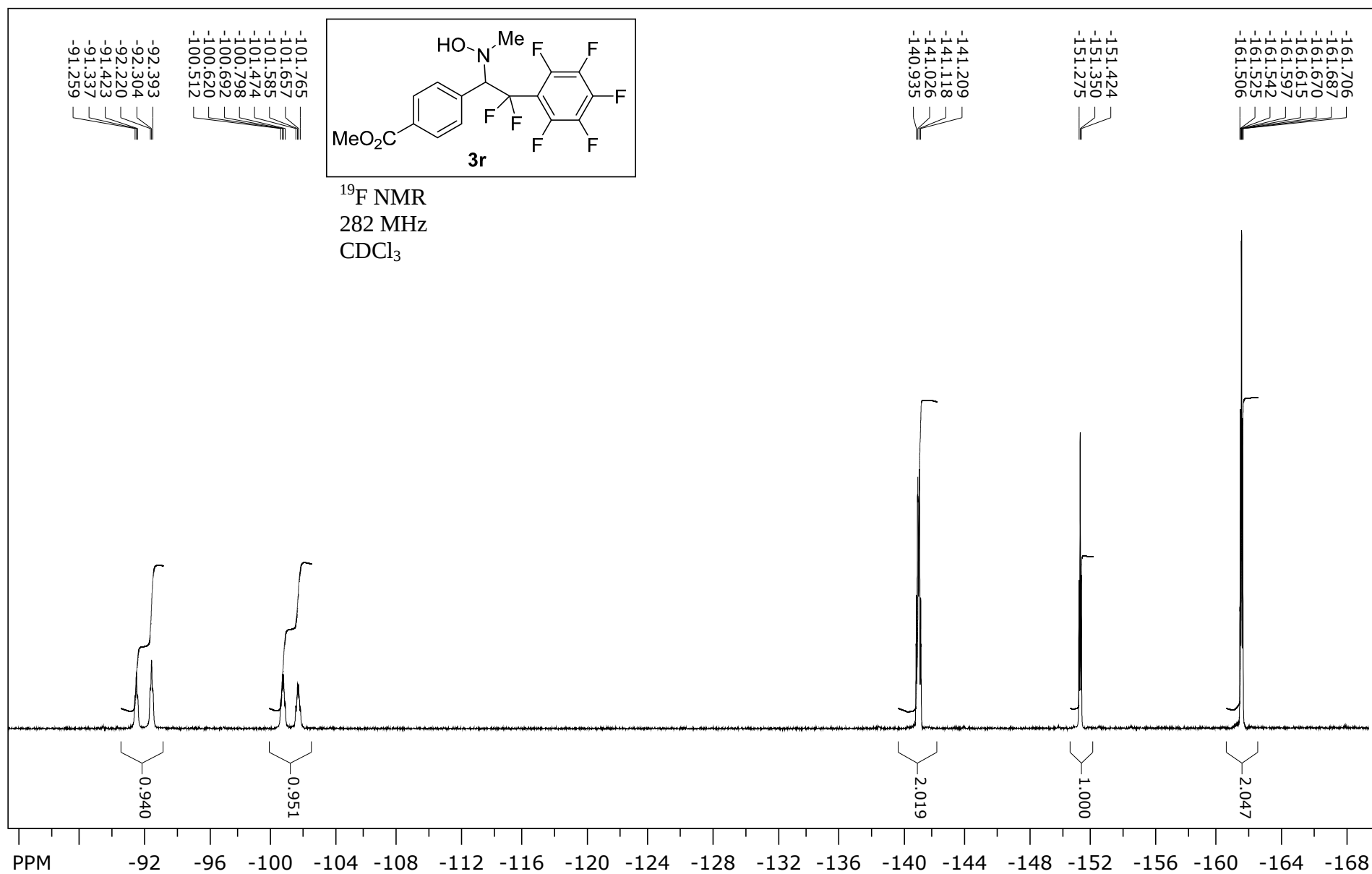


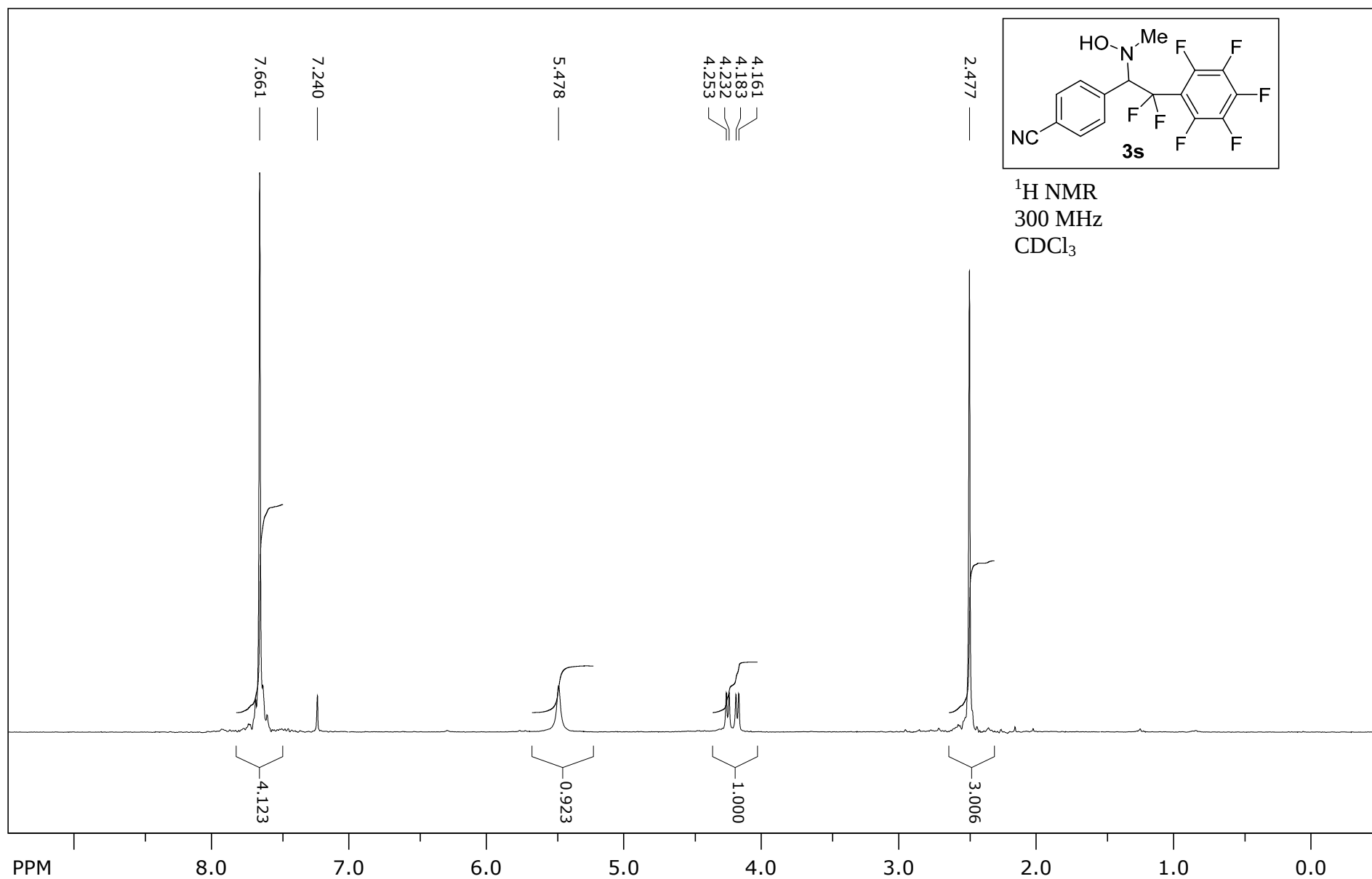


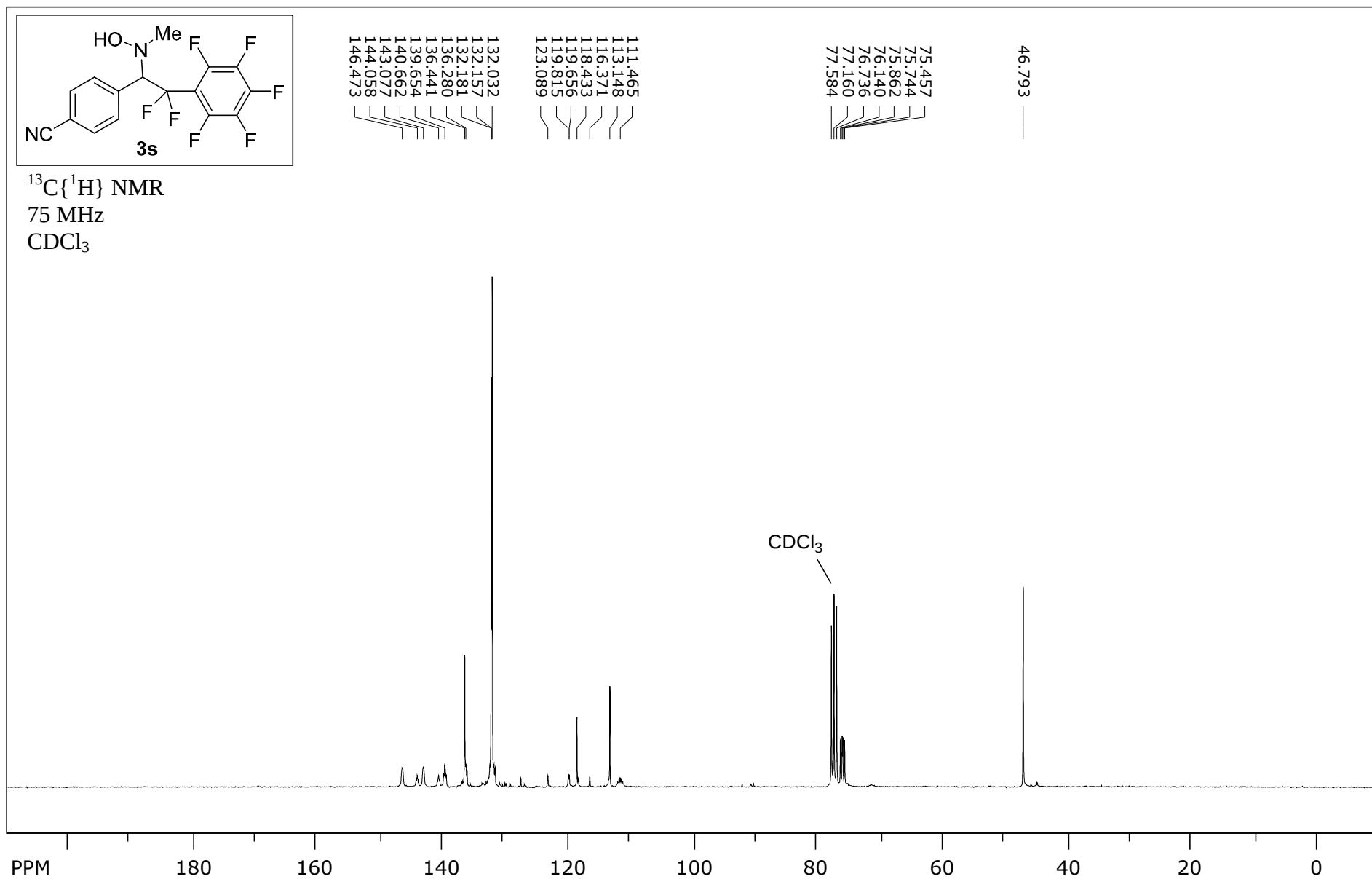


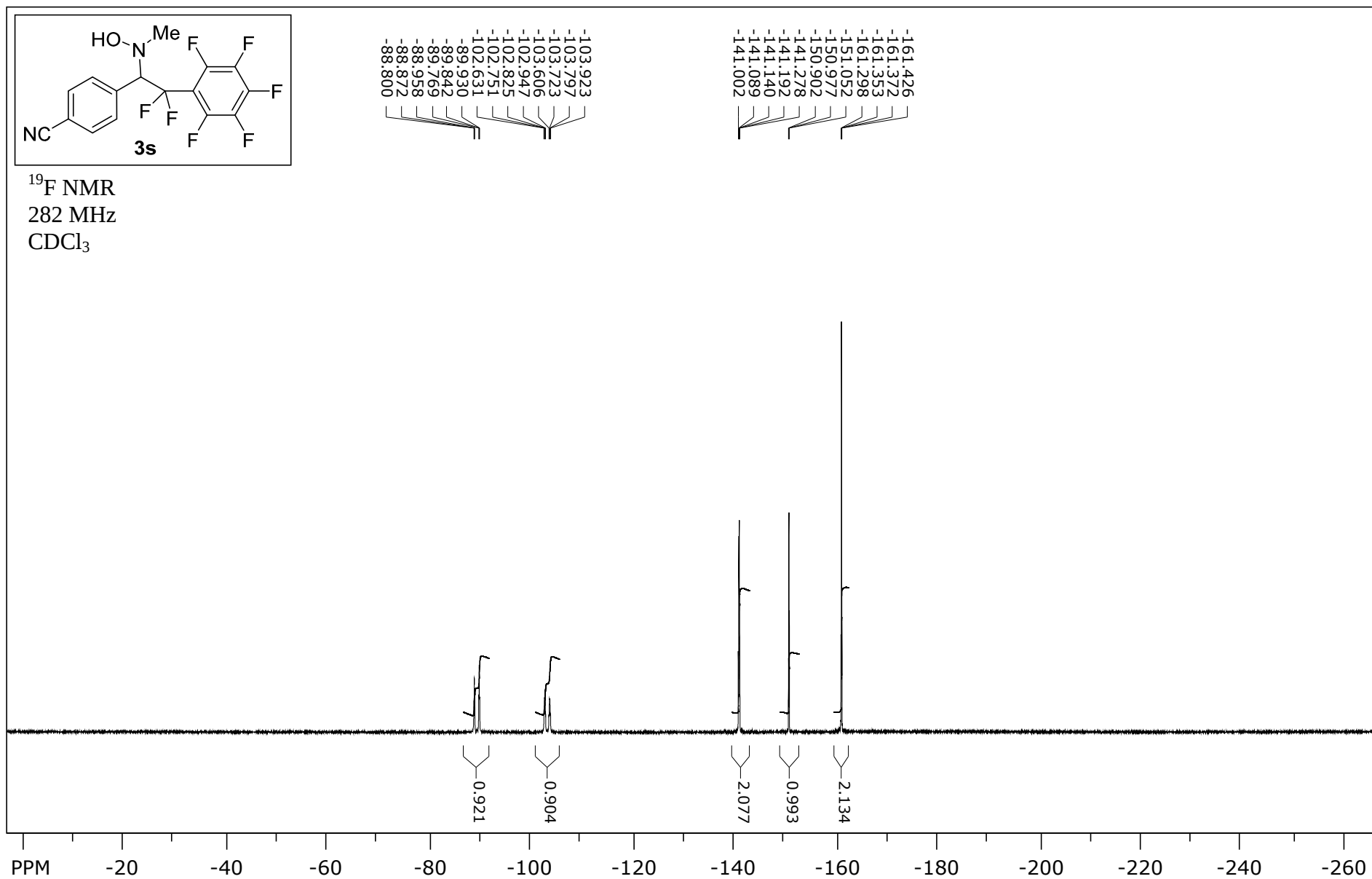


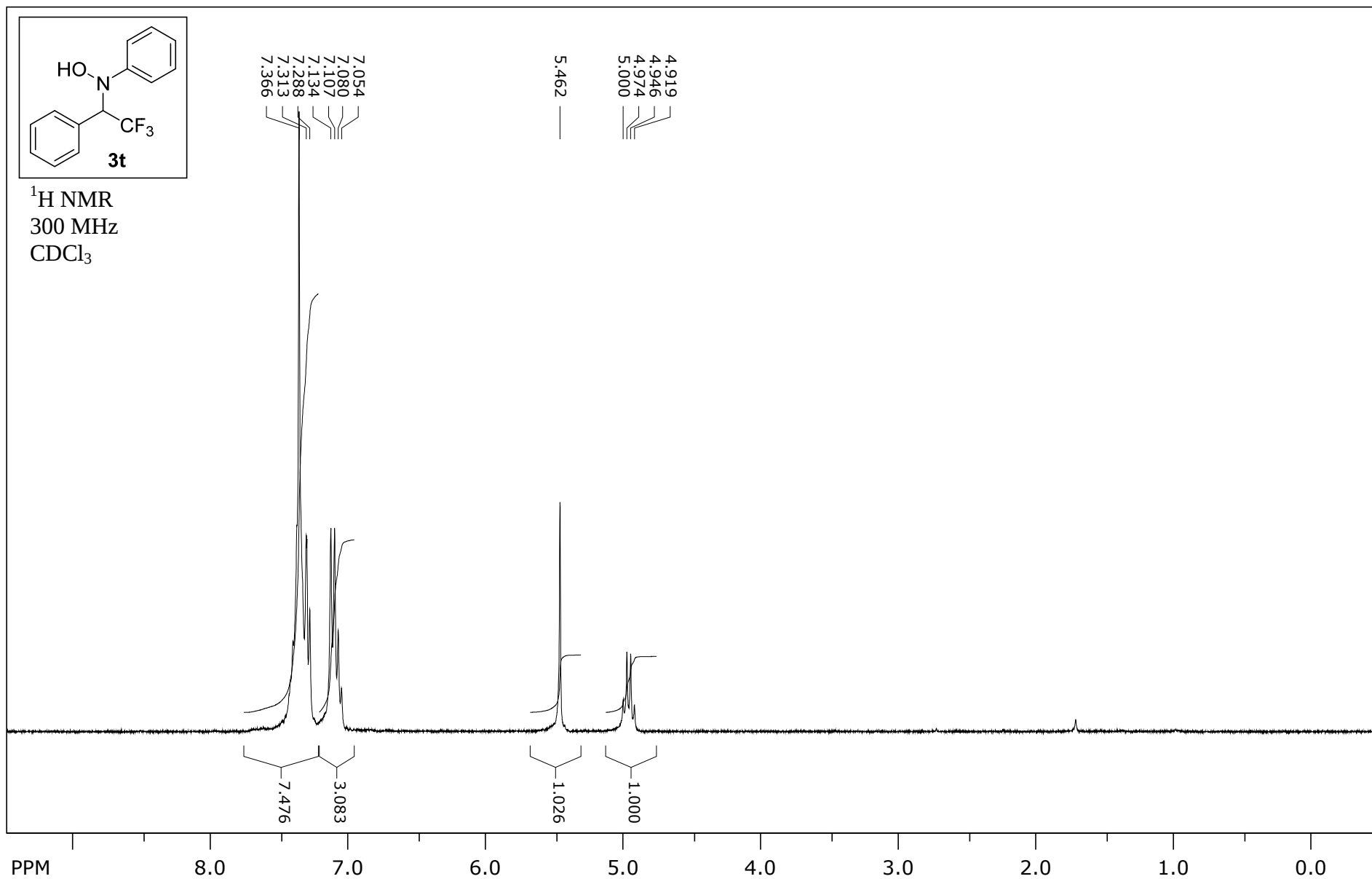


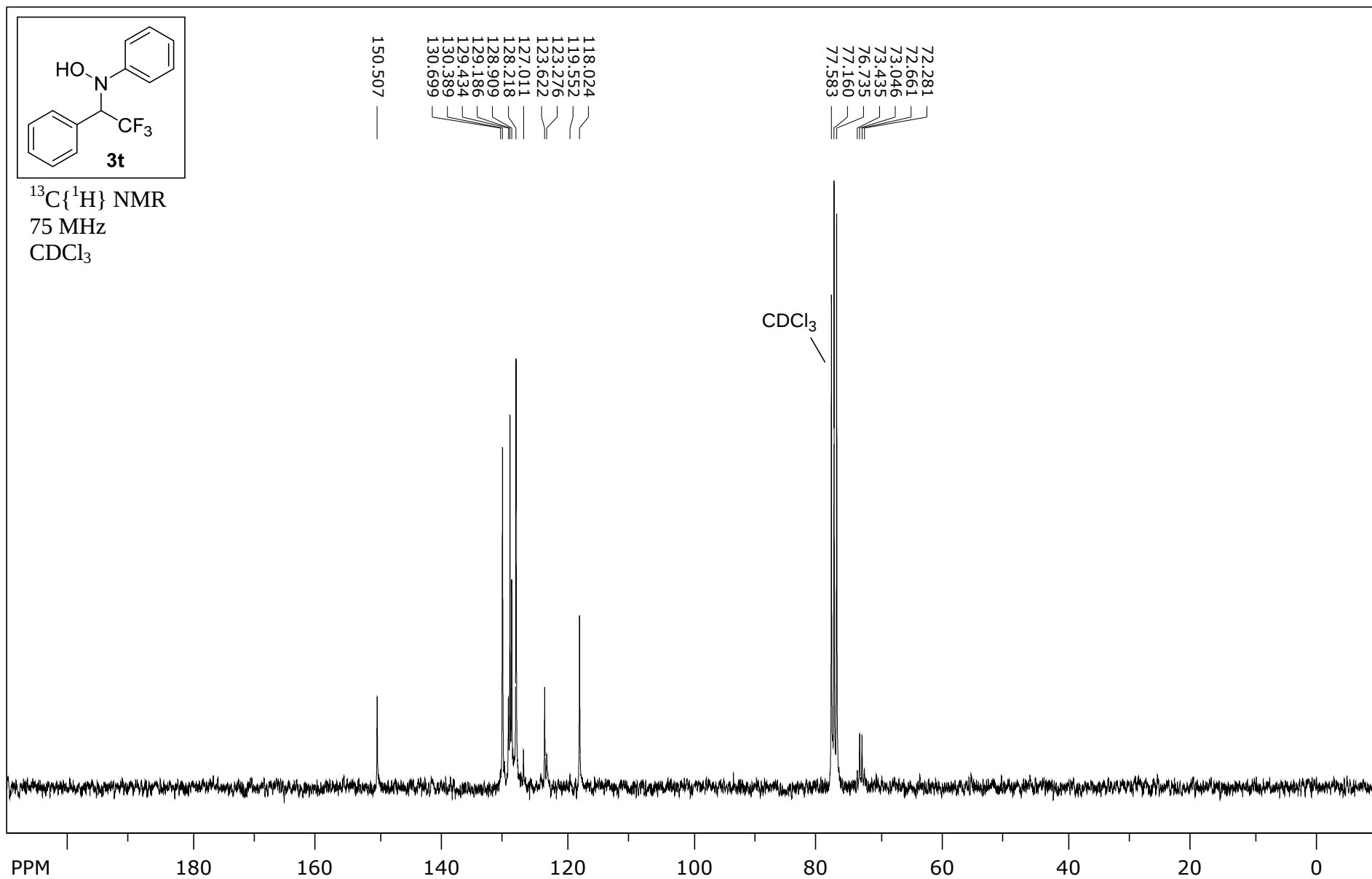


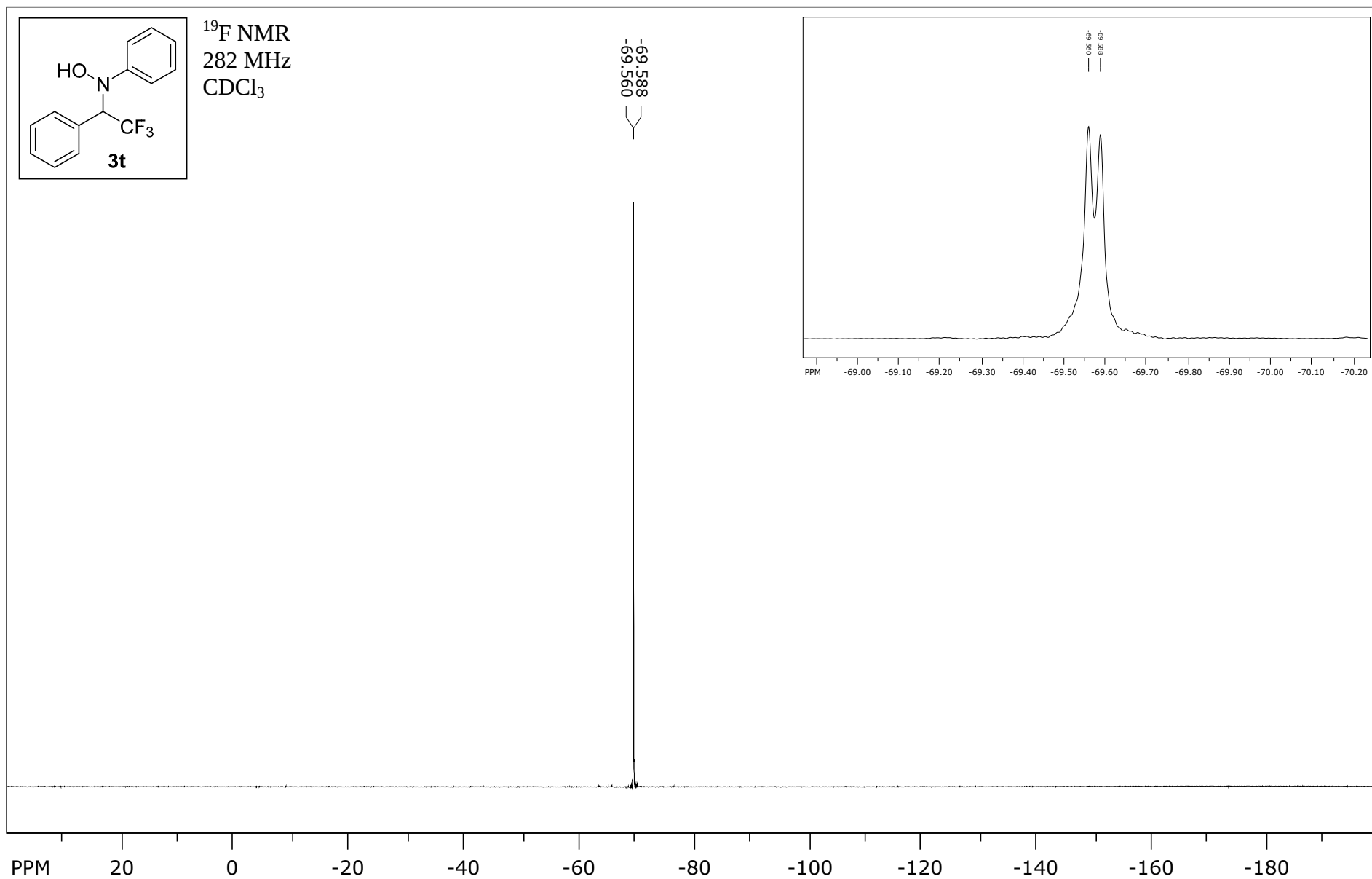


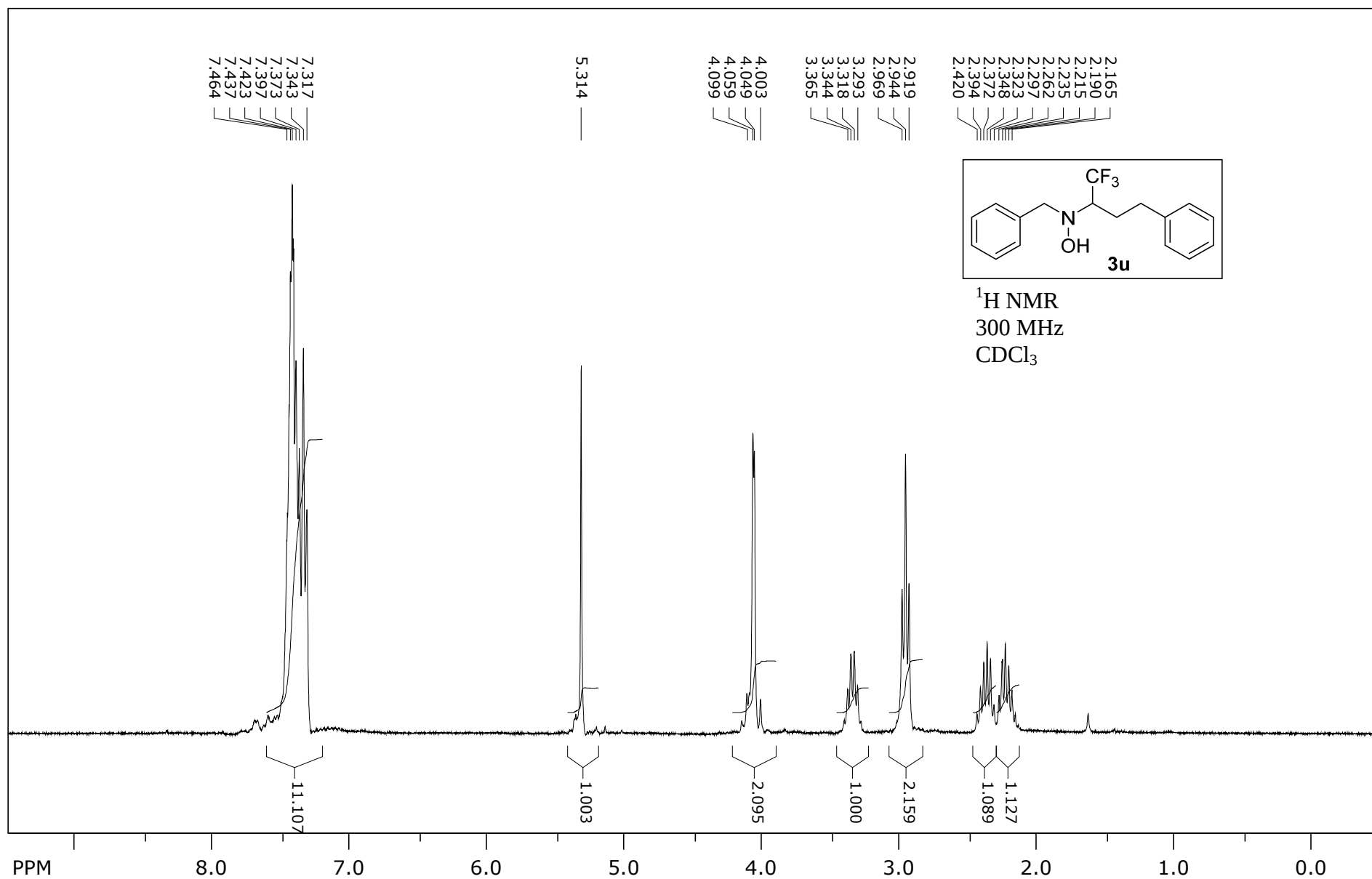


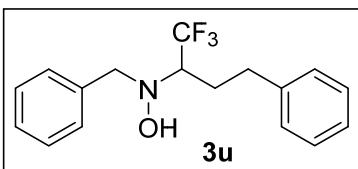




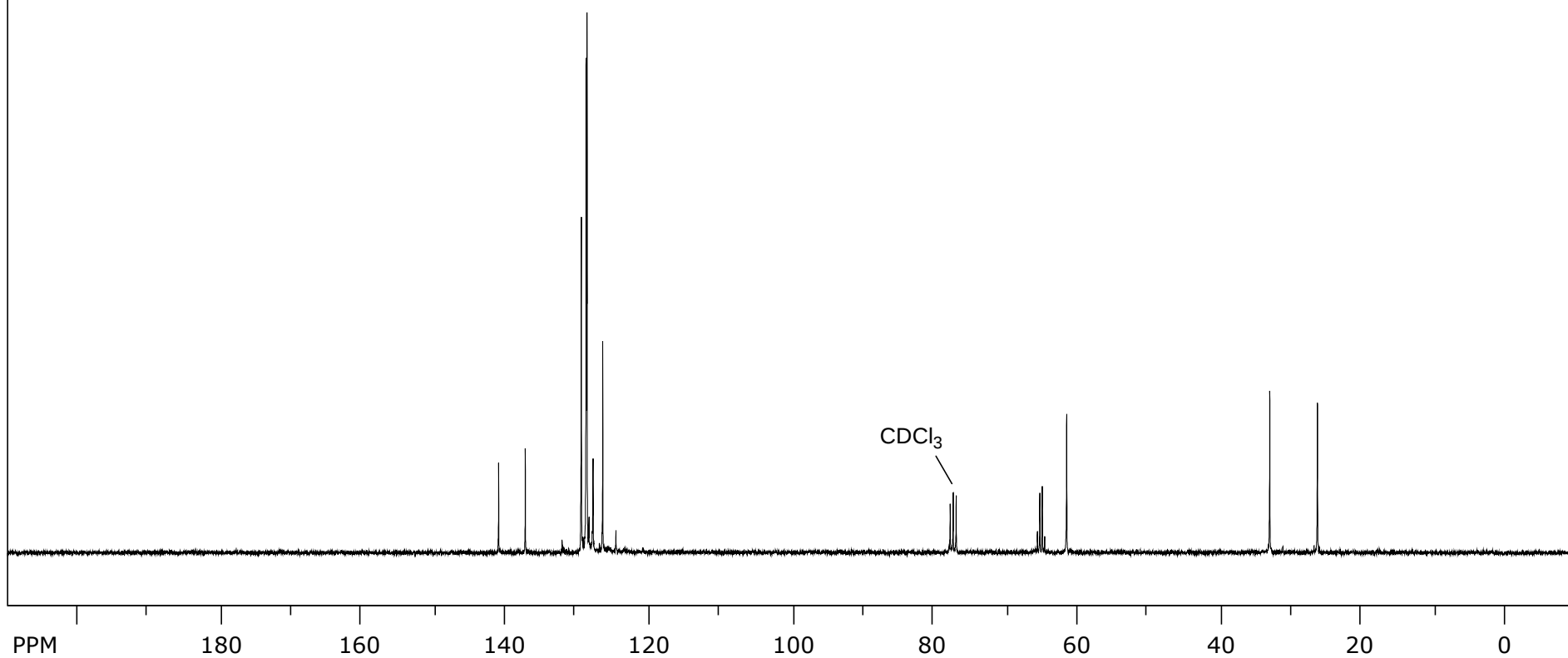


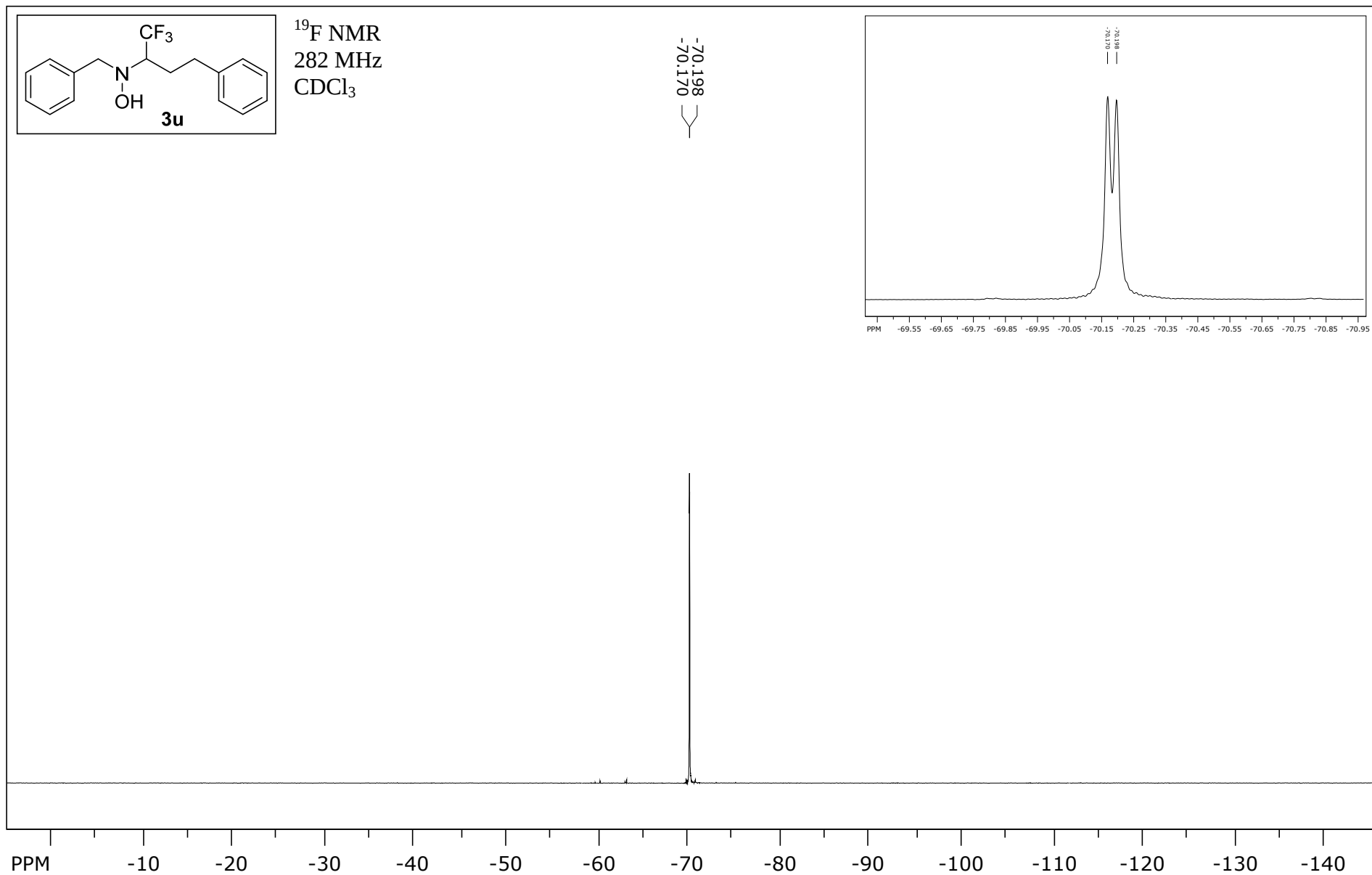


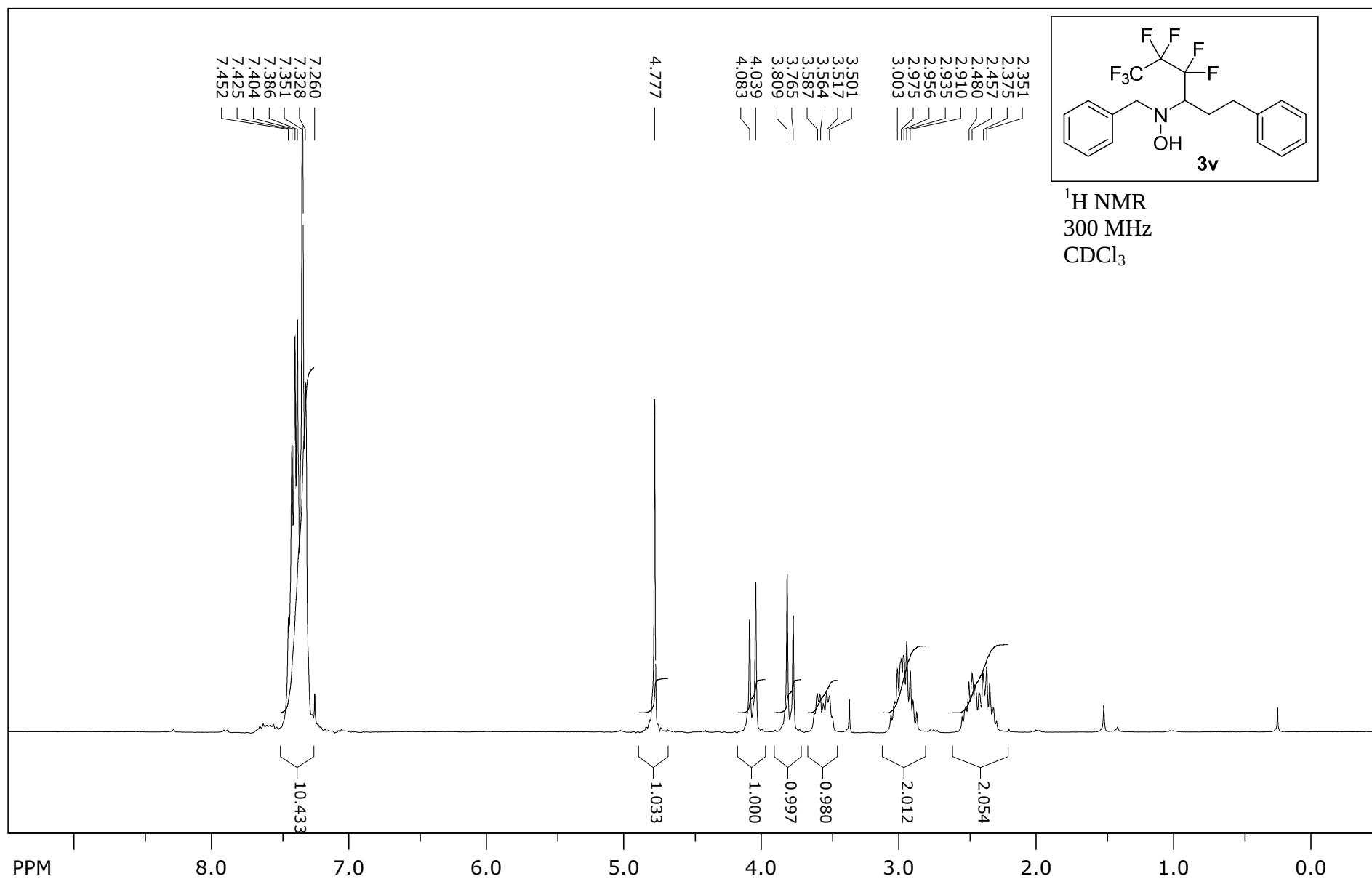


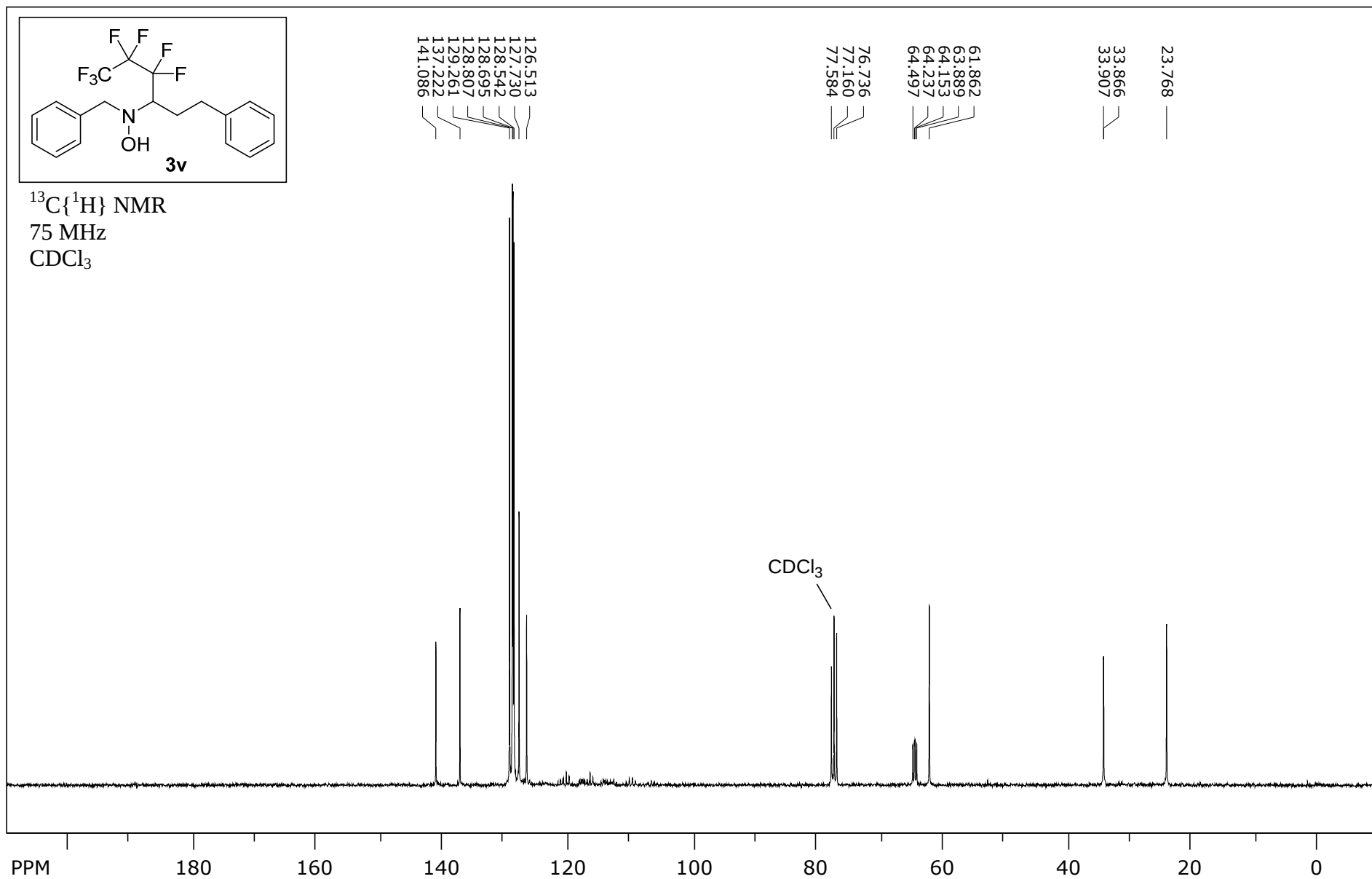
 $^{13}\text{C}\{^1\text{H}\}$ NMR

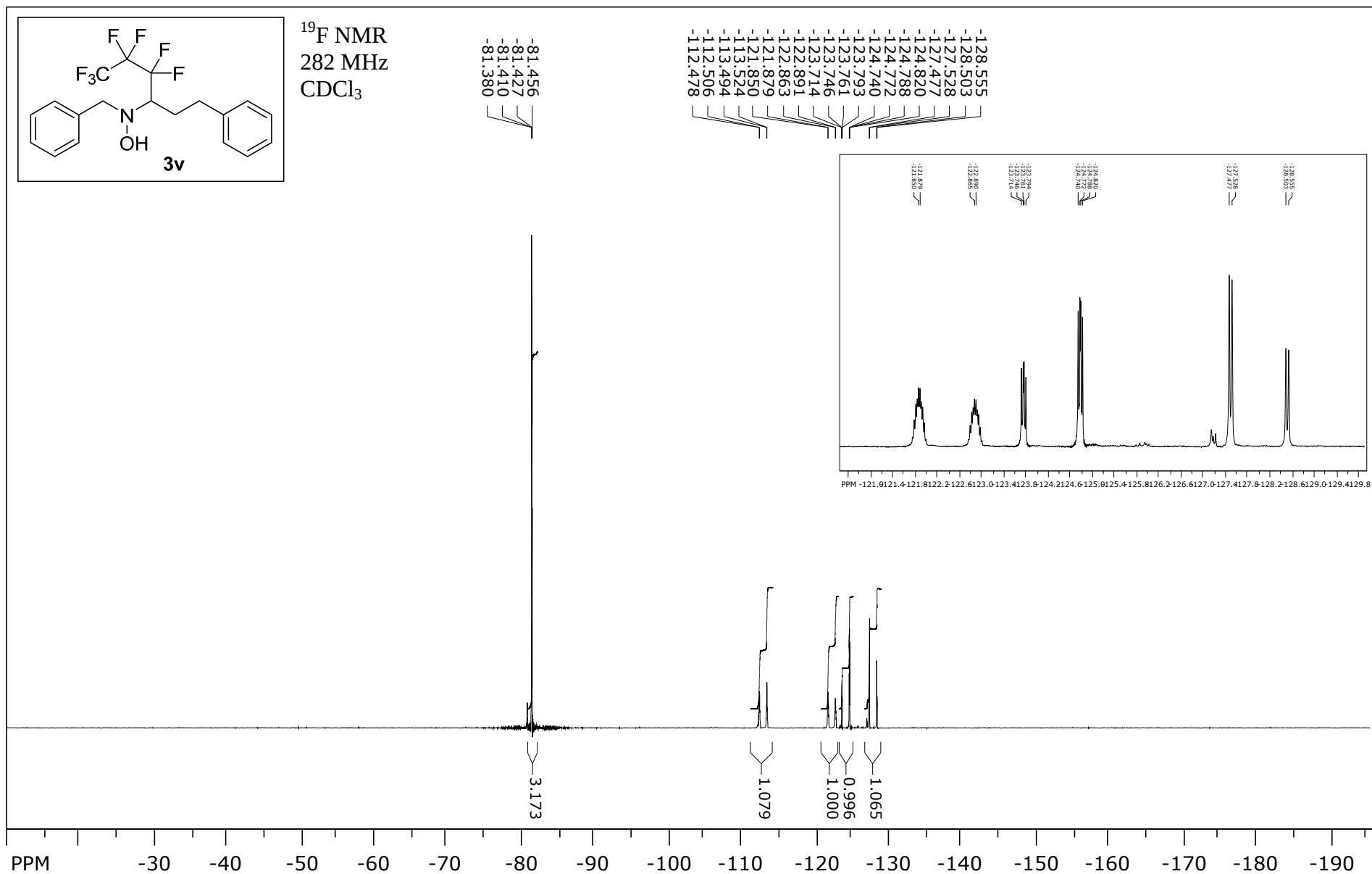
75 MHz

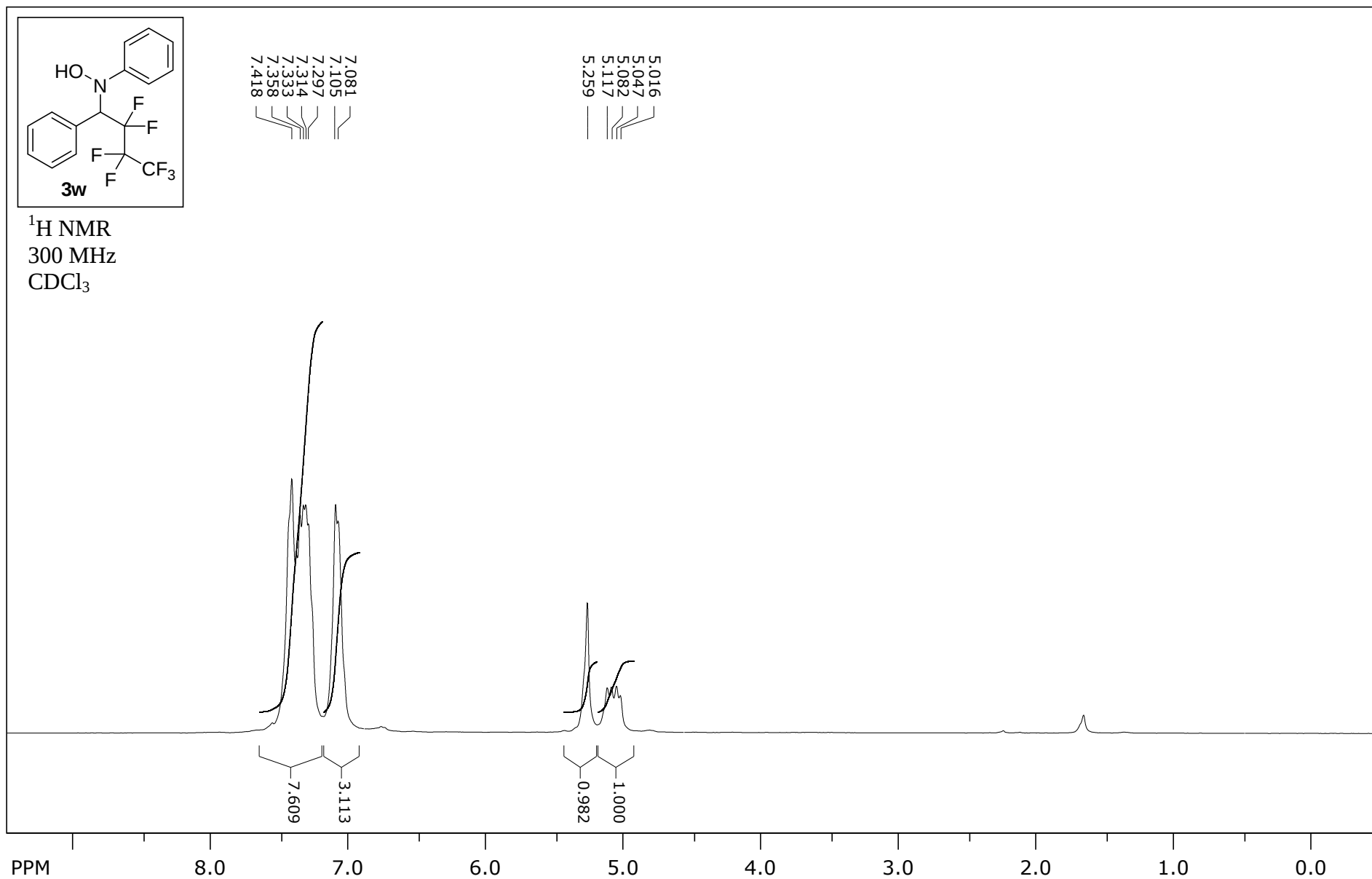
CDCl₃

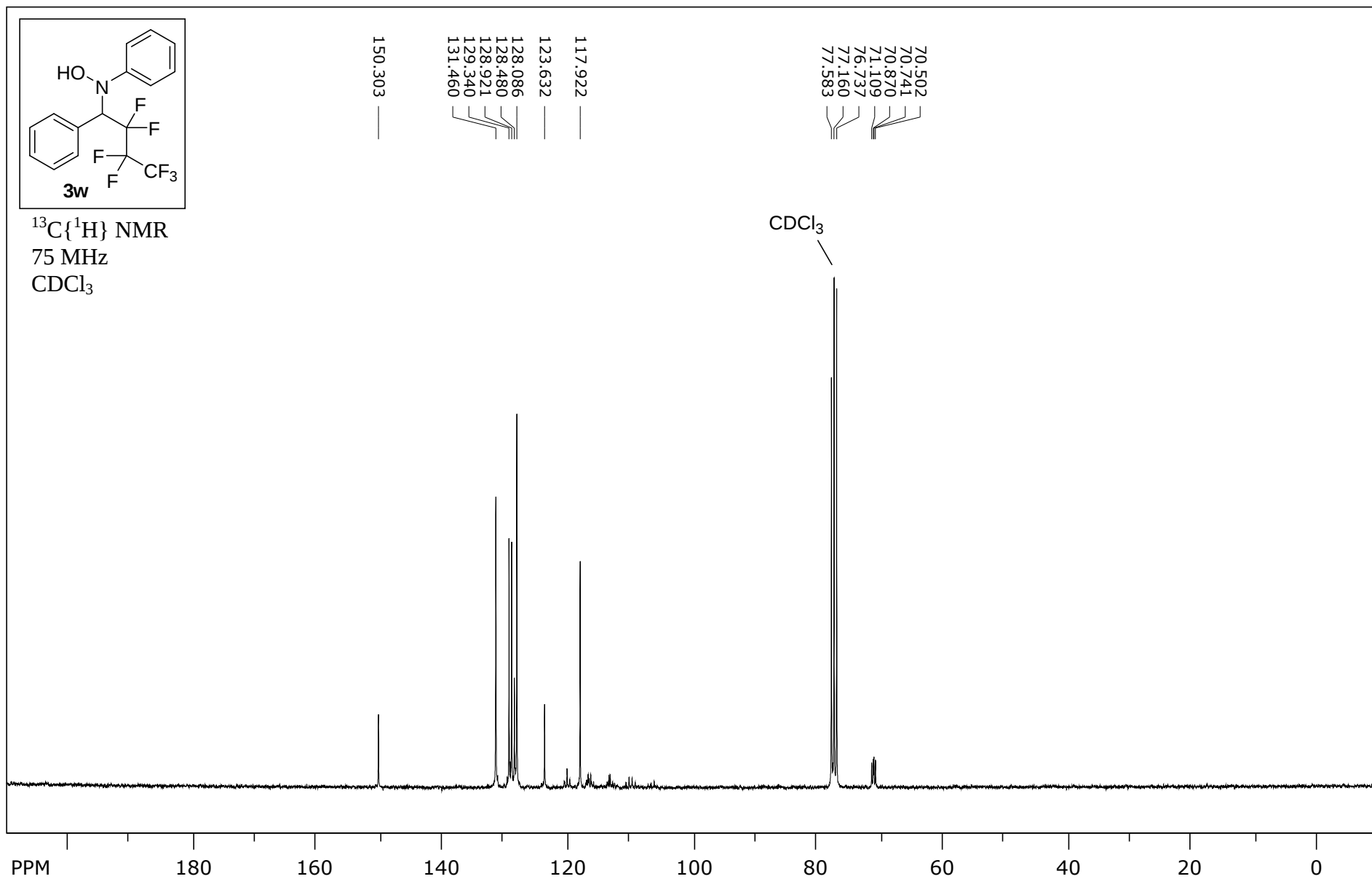


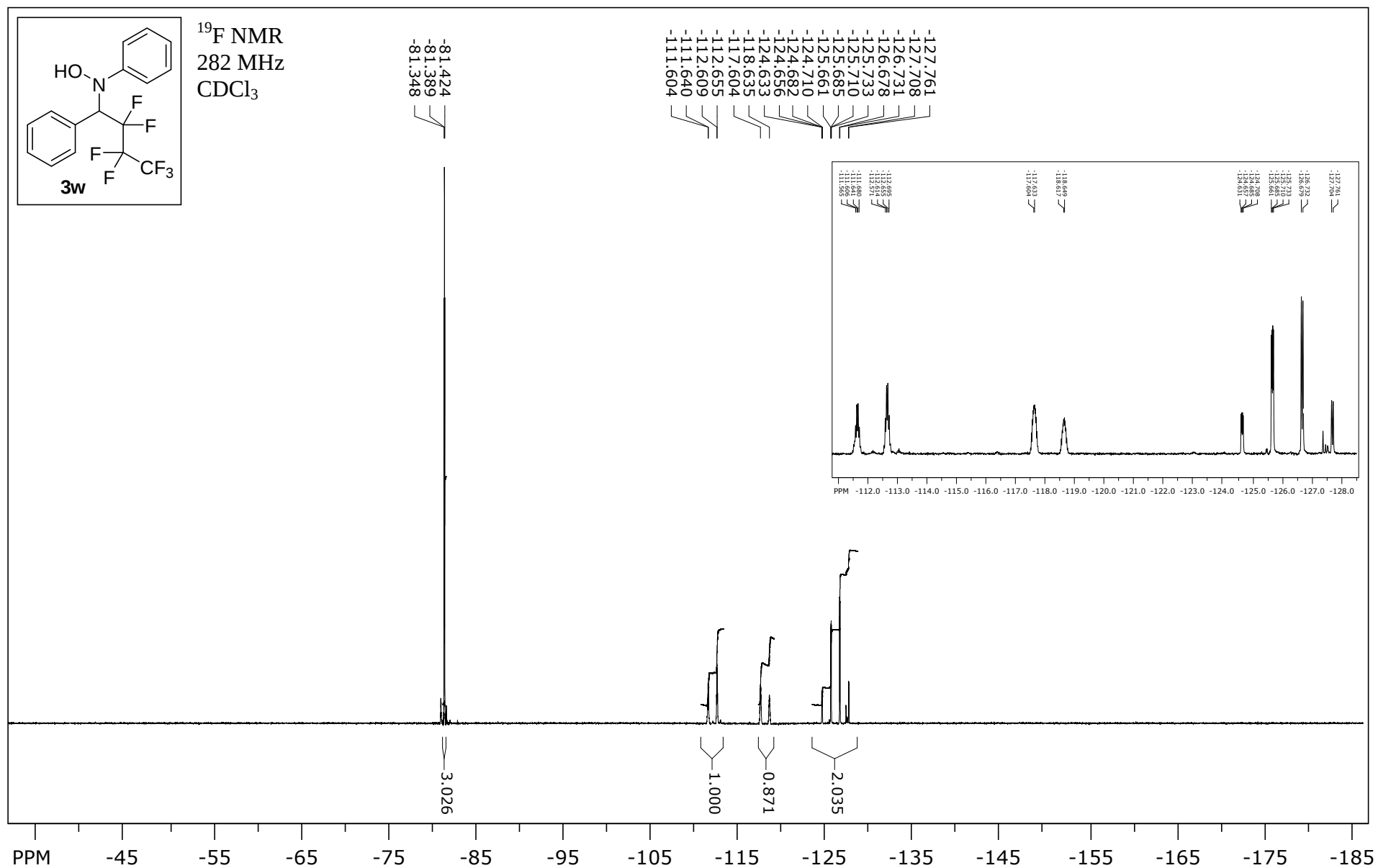


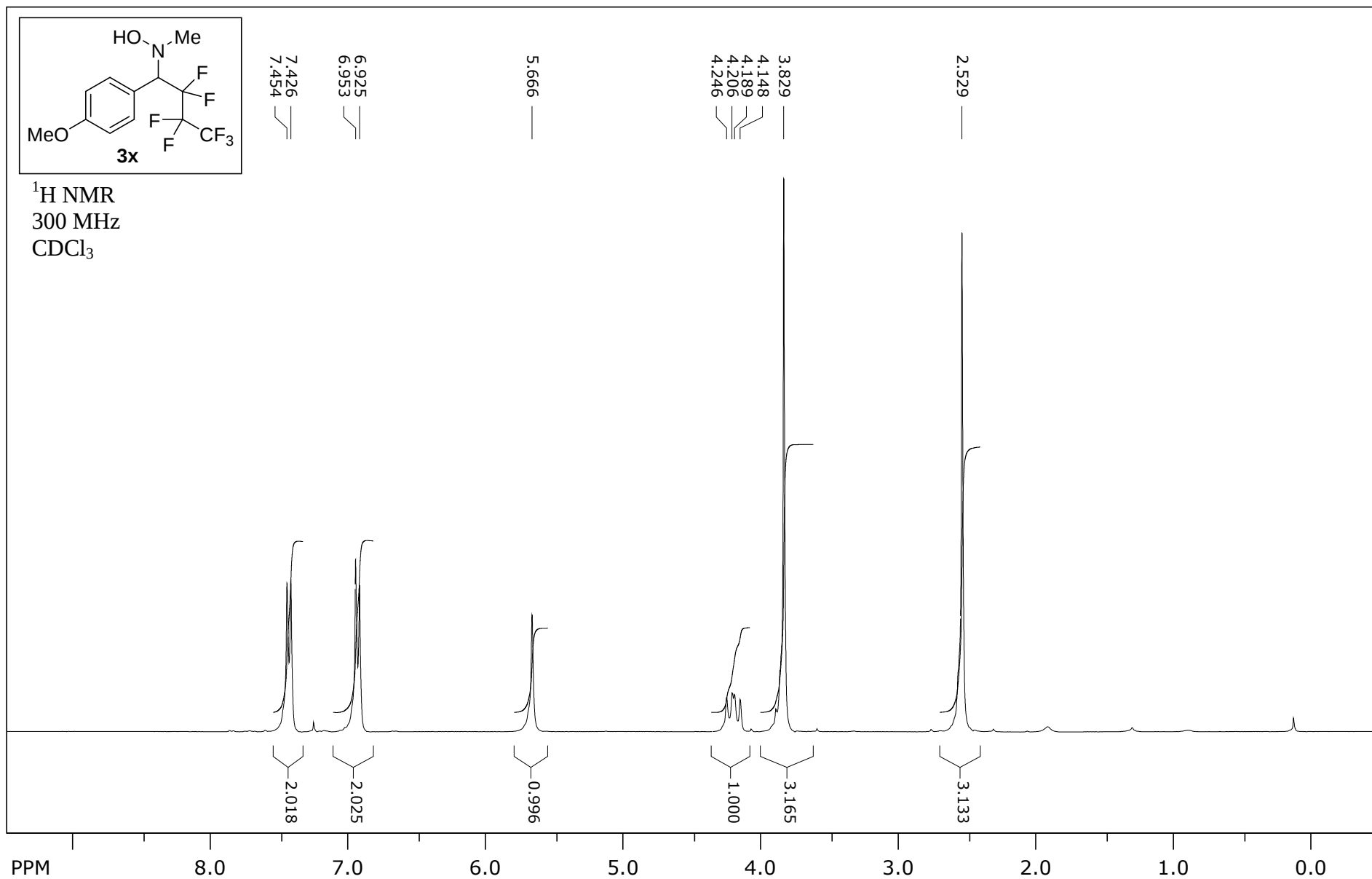


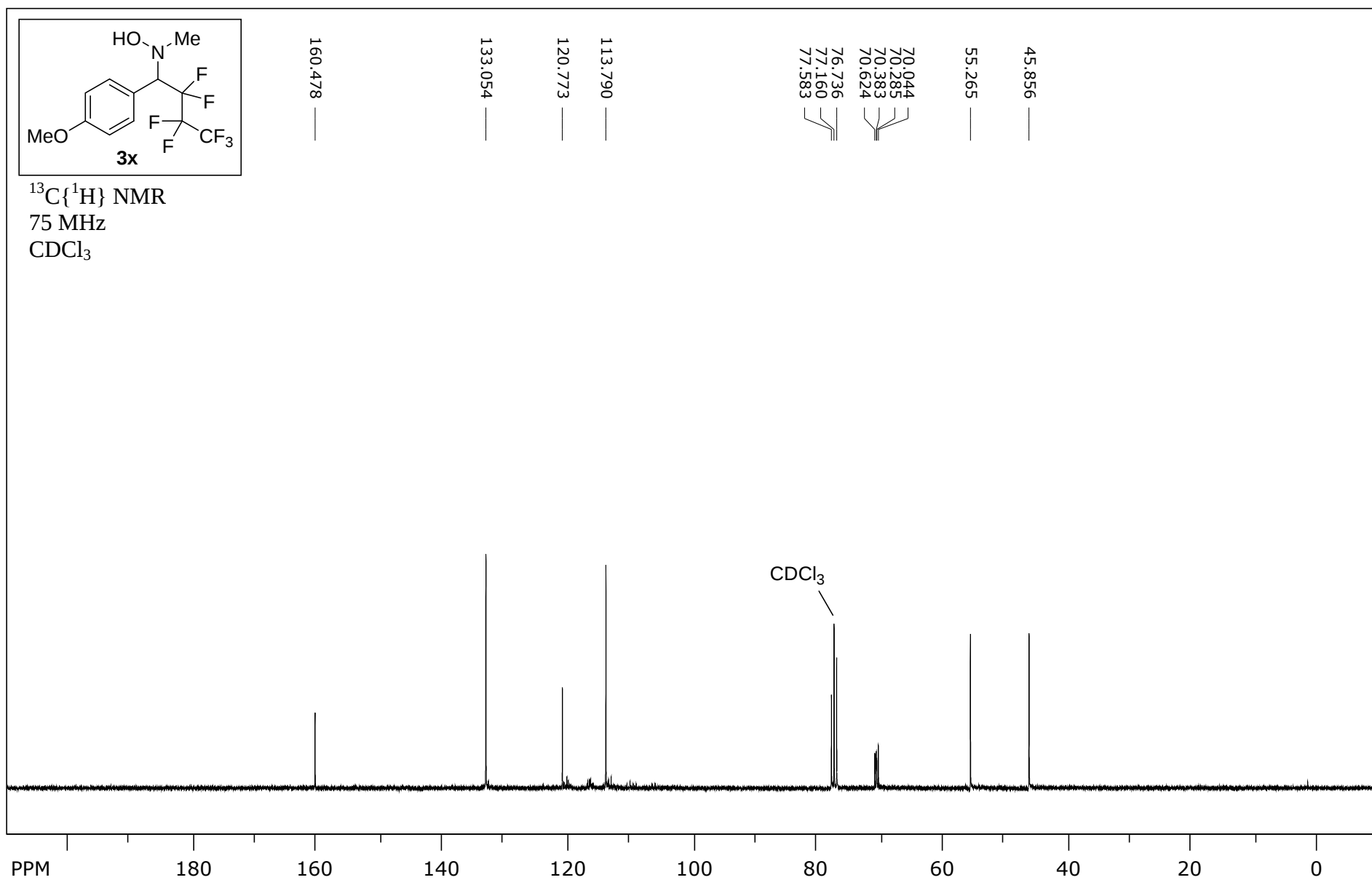


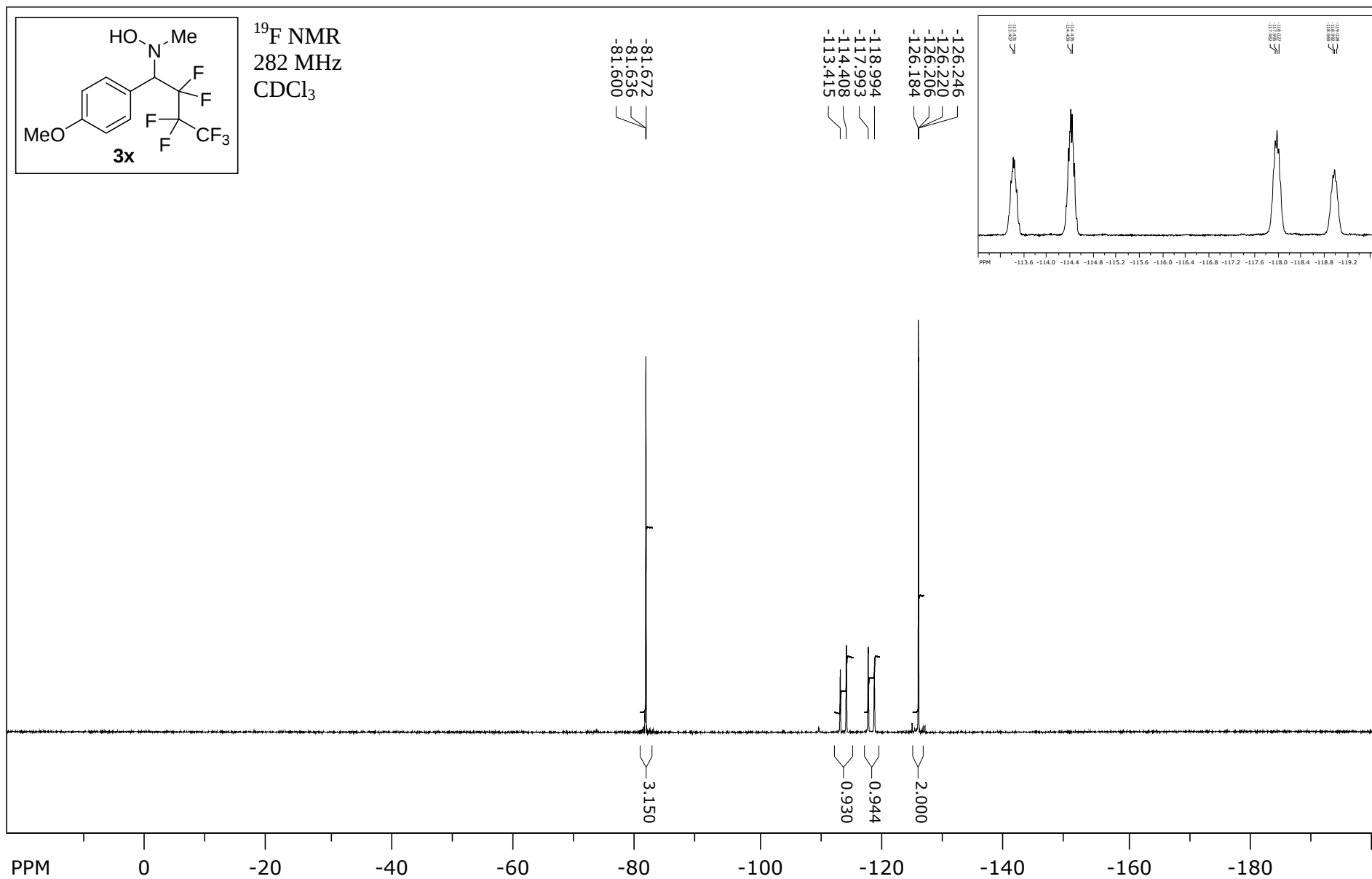


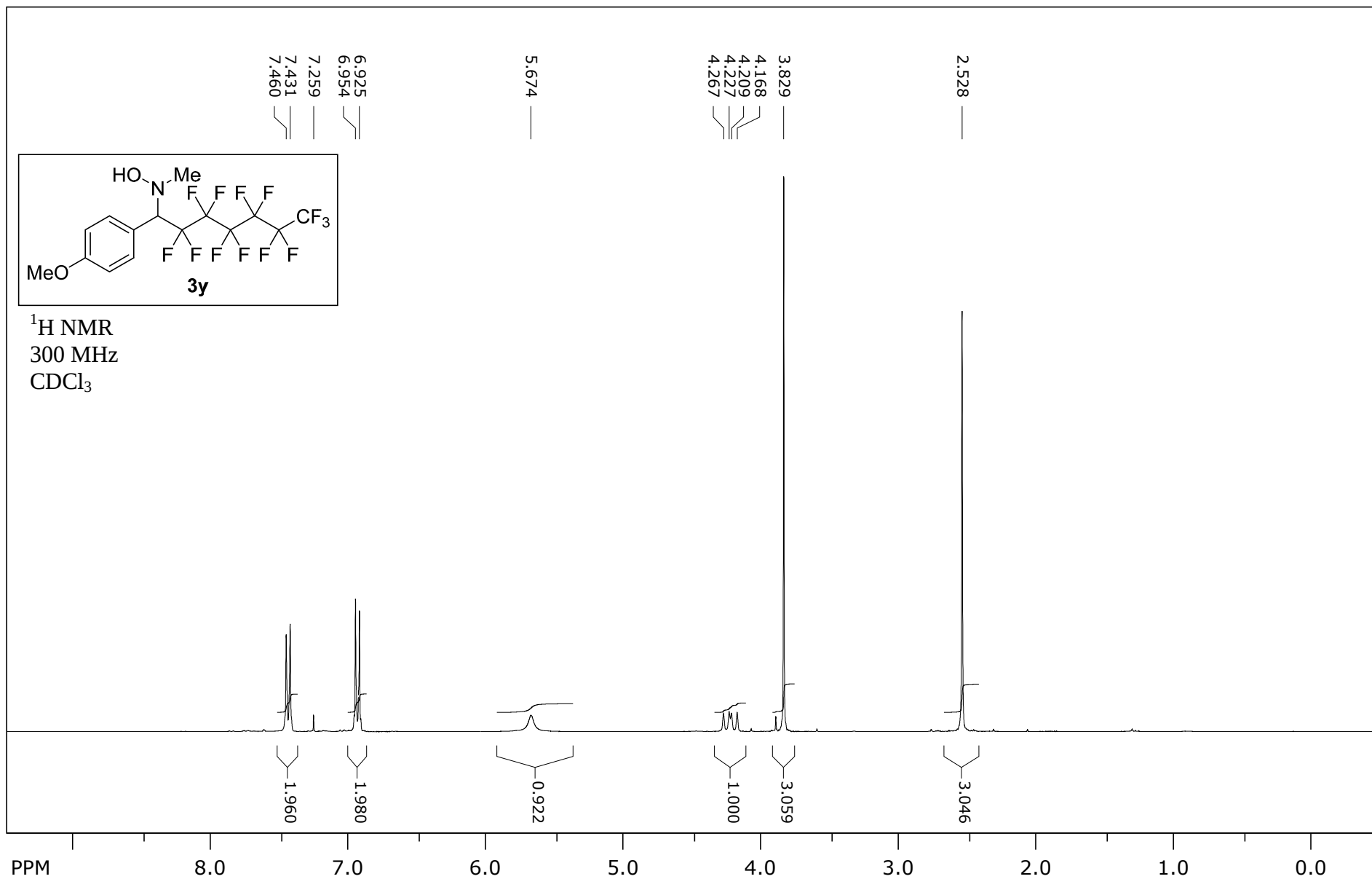


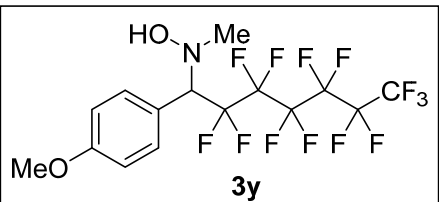












$^{13}\text{C}\{^1\text{H}\}$ NMR
75 MHz
 CDCl_3

